Drug Safety
https://doi.org/10.1007/s40264-019-00806-5

REVIEW ARTICLE

Drug-Induced Photosensitivity—An Update: Culprit Drugs, Prevention and Management

Kim M. Blakely[1] · Aaron M. Drucker[1,2] · Cheryl F. Rosen[1,3]

Abstract

Photosensitive drug eruptions are cutaneous adverse events due to exposure to a medication and either ultraviolet or visible radiation. In this review, the diagnosis, prevention and management of drug-induced photosensitivity is discussed. Diagnosis is based largely on the history of drug intake and the appearance of the eruption primarily affecting sun-exposed areas of the skin. This diagnosis can also be aided by tools such as phototesting, photopatch testing and rechallenge testing. The mainstay of management is prevention, including informing patients of the possibility of increased photosensitivity as well as the use of appropriate sun protective measures. Once a photosensitivity reaction has occurred, it may be necessary to discontinue the culprit medication and treat the reaction with corticosteroids. For certain medications, long-term surveillance may be indicated because of a higher risk of developing melanoma or squamous cell carcinoma at sites of earlier photosensitivity reactions. A large number of medications have been implicated as causes of photosensitivity, many with convincing clinical and scientific supporting evidence. We review the medical literature regarding the evidence for the culpability of each drug, including the results of phototesting, photopatch testing and rechallenge testing. Amiodarone, chlorpromazine, doxycycline, hydrochlorothiazide, nalidixic acid, naproxen, piroxicam, tetracycline, thioridazine, vemurafenib and voriconazole are among the most consistently implicated and warrant the most precaution by both the physician and patient.

Key Points

Photosensitive drug eruptions, including both phototoxicity and photoallergy, have been reported for a number of systemic medications.

This review provides a comprehensive overview of medications implicated in such reactions, including the clinical presentation for each medication and the evidence available to implicate them as true photosensitizers.

Improved reporting, including randomized control trials, will help to better characterize these reactions and provide a more comprehensive list of photosensitive medications for both the physician and patient.

✉ Cheryl F. Rosen
c.rosen@utoronto.ca

[1] Division of Dermatology, Department of Medicine, University of Toronto, Toronto, ON, Canada

[2] Division of Dermatology, Department of Medicine, Women's College Research Institute, Women's College Hospital, Toronto, ON, Canada

[3] Division of Dermatology, Toronto Western Hospital, Toronto, ON, Canada

1 Introduction

Photosensitive drug eruptions have been reported to represent up to 8% of cutaneous adverse events from drugs [1]. Such reactions, which can be classified as either photoallergic or phototoxic, occur after exposure to a photosensitizing drug, either topically or systemically, and either ultraviolet (UV) or visible radiation. Importantly, for a drug eruption to be considered photosensitive, it must meet the following criteria: (1) it occurs only in the context of radiation, (2) the drug or one of its metabolites must be present in the skin at the time of exposure to radiation and (3) the drug and/or its metabolite(s) must be able to absorb either visible or UV radiation. UVA radiation, which penetrates deeper into the dermis than UVB, is most commonly implicated in photosensitive drug eruptions, although UVB and visible light have been reported for specific medications [2].

Classically, photosensitivity reactions are classified based on their proposed mechanism of action into photoallergic and phototoxic reactions (Table 1). Attempts to distinguish the two can be made using clinical history and physical examination, as well as histopathology and clinical tests including phototesting and photopatch testing. However, distinguishing between phototoxicity and photoallergy in

Published online: 19 March 2019

Table 1 Differentiating features between photoallergic and phototoxic drug-induced photosensitivity (adapted from Gould et al. [88])

Feature	Photoallergy	Phototoxicity
Incidence	Low	High
Pathophysiology	Type IV hypersensitivity reaction	Direct tissue injury
Required dose of medication	Low	Usual dose to high
Required dose of radiation	Low	High
Onset after light exposure	> 24 h	< 24 h
Clinical appearance	Eczematous	Exaggerated sunburn reaction
Sensitization required	Yes	No
Localization	May spread outside exposed areas	Only exposed areas
Pigmentary change	Unusual	Frequent
Histology	Epidermal spongiosis, exocytosis of lymphocytes and a perivascular inflammatory infiltrate	Necrotic keratinocytes, predominantly lymphocytic and neutrophilic dermal infiltrate

an individual patient can be difficult, and usually does not affect management.

Photoallergic drug eruptions, in addition to meeting all the criteria for photosensitivity reactions outlined above, must demonstrate an immune-mediated mechanism of action. Similar to other type IV hypersensitivity reactions, not all persons exposed concurrently to both the drug and to radiation will experience the photosensitivity reaction. When a susceptible person does display a photoallergic reaction, typically it will present clinically as a predominantly eczematous eruption. Histopathologic features are identical to those seen in an allergic contact dermatitis, including epidermal spongiosis, vesiculation, exocytosis of lymphocytes and a perivascular inflammatory infiltrate [3].

Phototoxic drug eruptions are much more frequent than photoallergic reactions. Phototoxic drug eruptions are not immune-mediated, but instead result from direct cellular damage. As such, phototoxic reactions will occur in all individuals exposed to sufficient doses of both the drug and radiation of the appropriate wavelengths. Classically, phototoxic eruptions appear as exaggerated sunburn reactions with erythema, itching and burning. Histopathologically, necrotic keratinocytes are seen along with a predominantly lymphocytic and neutrophilic dermal infiltrate. Of note, both phototoxic and photoallergic drug eruptions may have a dermatitic appearance. Other manifestations of photosensitivity can include lichenoid eruptions, pseudoporphyria, onycholysis, erythema multiforme, hyperpigmentation and telangiectasia, as will be discussed in more detail with the various culprit medications below.

Not only are photosensitive reactions a cause of significant morbidity in affected individuals, but in some instances, pose a future risk for malignancy, specifically melanoma and keratinocyte carcinoma [4–9]. As such, awareness of these culprit drugs, and using appropriate measures to avoid these adverse reactions, is an important aspect of patient care when using photosensitizing medications.

In this review, which is an update from our original article published in 2011 [10], we discuss the diagnosis of photosensitivity reactions, culprit drugs, as well as prevention and management of these eruptions. We have not included reactions to topically administered drugs (e.g. sunscreens), and instead focus on reactions to systemically administered medications. We have also excluded drugs that cause photosensitivity as part of their desired mechanism of action (e.g. psoralens).

2 Diagnosis

Most cases of drug-induced photosensitivity can be diagnosed based on a detailed clinical history and physical examination, as well as knowledge of the classic groups of medications typically implicated in such reactions. That is, specialized testing is not necessary to make the diagnosis for most patients. However, investigations including phototesting may be important to differentiate drug-induced photosensitivity from other causes of photosensitivity, particularly where the relationship between onset of photosensitivity and drug ingestion is not clear. For patients with a suspected photosensitivity eruption, as with any dermatologic presentation, a thorough clinical history and physical examination should be performed. The interviewer should pay particular attention to medication history, with special consideration given to the temporal relationship of the eruption with the starting of any new medications. Additionally, a general review of systems should be performed to screen for diseases associated with photosensitivity, such as systemic lupus erythematosus. With photosensitive reactions, physical examination will often reveal a photodistributed eruption involving the face, V of the neck and extensor

forearms and hands. Areas typically spared include the upper eyelids, the base of skin folds (e.g. nasolabial folds), as well as the submental and posterior auricular regions, as these areas are relatively protected from sun exposure. In cases where there is no prior literature to support a photosensitive reaction to a given medication or where the diagnosis itself is in question, testing exists that may help to establish a diagnosis. Although several in vitro tests to assess the photosensitizing potential of certain medications in cultured cells exist [11–13], these are not practical or routinely available in the clinical setting. Clinically, the two tests that have proven most useful are phototesting and photopatch testing. With phototesting, the examiner uses artificial sources of UVB and UVA radiation to determine the minimal erythema dose (MED) for a patient under two conditions, while taking the medication in question and then following discontinuation of the medication. The MED is the lowest dose of radiation to produce uniform erythema on an exposed patch of skin. If the MED is lower while the patient is taking the medication, this supports compatibility with a drug-induced photosensitive eruption. Alternatively, photopatch testing is used to determine if a photoallergic reaction has occurred. The procedure is similar to patch testing used to assess allergic contact dermatitis. In photopatch testing, the examiner applies the medication in question, compounded in either petrolatum or alcohol, to the patient's back in duplicate. After 24 h, one set is irradiated with a dose of UVA below the MED. Twenty-four hours later, the irradiated and non-irradiated sites are examined for erythema, edema and vesiculation. If there is a reaction only at the irradiated site, it is suggestive of a photoallergic reaction. If there are equal reactions at both the irradiated and non-irradiated sites, it is suggestive of an allergic contact dermatitis to the medication. If there is a reaction at both the irradiated and non-irradiated sites, but the reaction is greater at the irradiated site, there may be both a contact dermatitis and a photoallergic reaction.

Obvious limitations exist with photopatch testing. Difficulties in interpretation of a positive reaction may arise when studying a medication in a topical formulation that is generally used systemically. Photopatch testing for the diagnosis of photo-induced cutaneous eruptions due to systemic medications has not been validated and may be negative even where the causative relationship between the drug and the photo-induced eruption is clear [14]. Thus, photopatch testing is most often reserved for topically applied medications and components of sunscreens. Quinine and chlorpromazine are among the few systemic medications where photopatch testing has been validated and is routinely performed. Photoscratch testing is a similar but less commonly used testing method that involves scratching the skin with a needle containing the compound for testing. Again, this method has been reported to have a high false-positive rate secondary to skin irritation [15] and is not validated for the majority of medications discussed in this review.

3 Photosensitizing Drugs

In this updated narrative review, we discuss the drugs that have been reported, in the English-language medical literature, to cause clinical photosensitivity. PubMed was the primary search engine utilized, and articles were filtered using the key search terms 'drug-induced photosensitivity', 'drug-induced photoallergy' and 'drug-induced phototoxicity'. Once articles were obtained, more specific searches including drug name (e.g. 'voriconazole and drug-induced photosensitivity') were also performed for each culprit medication.

As mentioned in our 2011 review, there are significant challenges associated with ascertaining the incidence of photosensitivity reactions to systemic medications. Such reactions are largely underreported, particularly for drugs that have been on the market for many years and are known photosensitizers. The literature describing photosensitivity reactions from systemic medications predominantly consists of case reports and case series. These comprise the majority of the data included in this review. More randomized, double-blind, placebo-controlled trials of possible photosensitizing medications using phototesting to detect changes in the MED to UVA would support clinical knowledge of a drug's photosensitizing potential. While this would greatly benefit this field and provide a more solid framework for patient education around specific medications and their potential adverse reactions, it is likely not a realistic proposition. However, improved reporting of cutaneous adverse events in randomized controlled trials, particularly distinguishing photosensitivity from the more generic 'rash', is more realistic and would be beneficial.

In light of these limitations, Table 2 contains a list of medications that are, in our opinion, important or common causes of photosensitivity. This list was derived based on the data compiled from this study as well as our clinical experience in the field. Importantly, this list is consistent with other studies on this topic, including a large systematic review recently published on drug-induced phototoxicity [16]. Tables 3, 4, 5, 6, 7, 8, 9 and 10 list medications, divided by therapeutic class, that have been reported to cause photosensitivity. For each medication listed, the evidence for its culpability in causing a photosensitivity eruption is given (whether phototesting, photopatch testing, or rechallenge testing was positive). We consider photopatch testing and rechallenge testing to be the strongest evidence available. Additionally, for each medication presented, the phototoxic or photoallergic clinical manifestations are discussed to better direct the physician when evaluating a patient with a suspected photosensitivity reaction.

Table 2 Common photosensitizing medications according to the authors' experience and literature review (in alphabetical order)

Amiodarone
Chlorpromazine
Doxycycline
Hydrochlorothiazide
Nalidixic acid
Naproxen
Piroxicam
Tetracycline
Thioridazine
Vemurafenib
Voriconazole

3.1 Antimicrobials

3.1.1 Tetracyclines

Tetracyclines are broad-spectrum antimicrobial agents exhibiting activity against a wide range of gram-positive and gram-negative bacteria, atypical organisms such as chlamydia, mycoplasma, rickettsia and protozoan parasites. They are perhaps the best recognized class of medications to cause photo-induced drug eruptions. Tetracycline and doxycycline have been reported to cause a variety of photosensitive rashes ranging from mild sunburn-like reactions with erythema and burning in sun-exposed areas to more widespread photodermatitis [17, 18]. Less frequently, solar urticaria [19], actinic granuloma [20] or lichenoid reactions [21] have been reported. In addition to skin manifestations, these medications are also reported to cause nail dystrophy with photo-induced onycholysis (i.e., nail plate detachment) and dyschromia. Minocycline is generally not considered to be a significant cause of photosensitivity, however photo-onycholysis has been reported [22]. Photo-induced onycholysis has now been reported for tetracycline [23–25], doxycycline [17, 26], minocycline [22] and lymecycline [27]. In children, severe cases of doxycycline-induced photo-onycholysis have been reported with involvement of all 20 nails [28] and at doses as low as 20 mg per day [29]. Importantly, nail effects can be delayed in presentation up to 2 weeks following sun exposure [30].

At least for doxycycline, phototoxic eruptions are thought to be due to radiation in the UVA1 spectrum (340–400 nm) and appear to be dose dependent [31]. Studies from the UK have demonstrated that phototoxicity to doxycycline occurs at single doses of 100, 150 and 200 mg at rates of 3, 20 and 42%, respectively [31]. The true incidence of photosensitive reactions in patients taking tetracycline class antibiotics is difficult to ascertain, as these reactions are felt to be underreported. For doxycycline, the incidence reported in the literature range from as low as 3% [31] to as high as 16% [32].

Skin cancer risk associated with use of these medications has been explored. In a study based on two large US cohorts, tetracycline use increased the risk of basal cell carcinoma by 11%, with no significant increase in the risk of squamous cell carcinoma or melanoma [33].

3.1.2 Nalidixic Acid and Fluoroquinolones

The antibiotic nalidixic acid and its derivatives, the fluoroquinolones, are believed to cause both phototoxic and photoallergic eruptions [34–37]; however, the incidence and severity of reactions differ greatly between the various members of this class.

Nalidixic acid is a known photosensitizer, and one of the medications associated with the development of fragile skin and the characteristic blistering of pseudoporphyria in sun-exposed areas [34, 37–39]. However, the clinical manifestations of fluoroquinolone phototoxicity are poorly detailed in the literature. Biochemical studies have demonstrated that derivatives of this class of medications that contain a halogen group at their position 8, including sparfloxacin, lomefloxacin and clinafloxacin, were found to have the greatest phototoxic properties [40–45]. Alternatively, those with a hydrogen group at this position, including ciprofloxacin and levofloxacin, have only mild phototoxic potential [41, 44, 46, 47]. Finally, those with a methoxy group at this position, as is the case with moxifloxacin, are more photostable and the least phototoxic [48, 49]. This is reflected in clinical studies that have demonstrated that some of the most frequently prescribed fluoroquinolones, including ciprofloxacin, levofloxacin and moxifloxacin, have very low photosensitizing potential when administered to healthy patients [46, 48, 50, 51]. When photosensitivity to a fluoroquinolone does occur, there is typically a return to baseline 1 week after the drug has been discontinued. However, persistent sequalae from phototoxicity have been reported secondary to the use of ciprofloxacin in a lung-transplant recipient on long-term immunosuppressive therapy [52]. Case reports of photo-induced purpura have been reported secondary to the use of both ciprofloxacin [53] and levofloxacin [54]. One case-control study including 1318 melanoma patients and 6786 controls found that quinolone use was associated with an increased risk of melanoma (odds ratio 1.33; 95% confidence interval 1.01–1.76) [55]. Further studies are required to establish whether this association is causal and specifically whether it is related to the phototoxic properties of quinolones.

3.1.3 Other Antibacterial Agents

Cefotaxime and ceftazidime, third-generation cephalosporins, have been implicated in photo-induced drug eruptions [56, 57]. In the case of cefotaxime, photosensitivity manifested as photodistributed telangiectasia, while ceftazidime caused increased susceptibility to sunburn.

Table 3 Antimicrobial medications reported to cause photosensitive drug eruptions

Subclass	Drug	Evidence
Tetracyclines	Tetracycline	PT [19]
	Doxycycline	PT [18], PP [18], RC [18]
	Minocycline	–
	Lymecycline	–
Nalidixic acid and the fluoroquinolones	Nalidixic acid	PT [37]
	Ciprofloxacin	PT [46]
	Sparfloxacin	PT [45]
	Ofloxacin	PT [47]
	Lomefloxacin	PP [43], RC [43], PT [48]
	Levofloxacin	–
	Moxifloxacin	–
	Clinafloxacin	–
Beta-lactams	Cefotaxime	PT [56]
	Ceftazidime	–
Miscellaneous antibiotics	Dapsone	PP [62], RC [59, 61, 63]
	Trimethoprim	RC [64]
Antituberculous	Isoniazid	PP [65], RC [65]
	Pyrazinamide	RC [66]
Antifungals	Voriconazole	PT [74]
	Itraconazole	PT [78], RC [78]
	Ketoconazole	–
	Griseofulvin	PT [82]
	Terbinafine	PT [87]
Antimalarials	Quinine	PP [91, 92], PT [90], RC [89, 93]
	Quinidine	PP [166], PT [163], RC [163]
	Chloroquine	PT [99], PP [99]
	Hydroxychloroquine	PT [97, 98], PP [98]
	Atoraquone/proguanil (Malarone)	PP [100]
Antiretrovirals	Efavirenz	PT [105], PP [105, 106]
	Tenofovir	PP [108]

PP photopatch testing, *PT* phototesting, *RC* rechallenge, – indicates test not done or test negative

Dapsone is a sulfone antibiotic and anti-inflammatory agent that has been implicated in both phototoxic and photoallergic drug eruptions [58–62]. This has been confirmed both by oral drug rechallenge and photopatch testing [61–63]. Trimethoprim, an antibiotic often used in combination with sulfamethoxazole, has also been reported to cause photosensitive in a single case report with positive rechallenge data [64].

Isoniazid and pyrazinamide, antibiotics used in the treatment of tuberculosis, have been implicated in causing photosensitive dermatoses. Isoniazid may cause a lichenoid eruption, and its photosensitizing effects have been confirmed by photopatch and rechallenge testing [65]. Pyrazinamide photosensitivity has been confirmed by rechallenge testing [66].

3.1.4 Antifungals

Voriconazole is a broad-spectrum triazole antifungal agent used in the treatment of invasive fungal infections. Although it is typically well tolerated, serious side effects including photosensitivity reactions have been reported. In fact, a recent literature review reported that voriconazole is the second most commonly reported culprit in phototoxicity reactions [16].

Reports of voriconazole photosensitivity range from classic phototoxicity patterns, to cheilitis, pseudoporphyria and photo-onycholysis [67–75]. The majority of reports in the literature occur in patients receiving long-term prophylactic therapy, with photosensitive eruptions occurring months after starting voriconazole therapy. While the acute photodermatitis usually resolves on discontinuation of the

drug, there are multiple reports of photoaging as well as the development of melanoma and squamous cell carcinomas in areas previously affected by the photosensitive eruption [6, 8, 9]. Importantly, these sequalae have been reported in paediatric patients treated with voriconazole [76, 77] and represent an important aspect of ongoing surveillance for these patients.

Itraconazole, another triazole antifungal agent, has also been reported to cause photosensitivity in a predominantly phototoxic pattern [78, 79]. The report detailed erythema, edema and vesicles on sun-exposed areas following a 5-day course of oral therapy for candidiasis that could be reproduced on rechallenge. Photodermatitis has also been reported with ketoconazole [80] but not fluconazole. One patient developed a phototoxic response to voriconazole that cleared within 6 weeks of substitution to fluconazole, suggesting potentially little or no cross-reactivity of this adverse photosensitive reaction [72].

Other than the azoles, few photosensitive reactions have been reported for other antimycotics. Griseofulvin is not thought to be a potent photosensitizer although it has been reported in the literature [81–83]. UVA has been implicated in griseofulvin-induced photosensitivity that may interfere with porphyrin metabolism, although further studies are required to confirm this theory [84–86]. There is also a single case report describing the development of solar urticaria in a patient taking terbinafine [87].

3.1.5 Antimalarials

Quinine and quinidine have been reported to cause both photoallergic and phototoxic reactions [88]. Quinine causes a photosensitive dermatosis that has been described as having several different morphological appearances including edematous, eczematous and lichenoid. Photo-onycholysis has also been described [89–94]. Photosensitivity from quinine may be persistent, which has been demonstrated experimentally and clinically [90, 91]. In the 1987 study by Ferguson et al., both patients who underwent photochallenge testing had a positive reaction. While it has not been seen clinically, experimental data from photopatch testing suggest that quinine and quinidine may cross-react with regard to photosensitivity [95].

Chloroquine and hydroxychloroquine are antimalarial drugs often used in dermatology for their photoprotective effects in photosensitive conditions such as polymorphous light eruption and systemic lupus erythematosus. Paradoxically, rare reports have been published confirming drug-induced photodermatoses induced by these medications, confirmed by phototesting and photopatch testing [96–99]. These reactions typically occur within days to weeks of starting these medications and resolve after discontinuation.

Most recently, a phototoxic reaction has been reported for the combination of atovaquone and proguanil (Malarone), a medication commonly prescribed for malaria prophylaxis [100]. In this case report, the patient developed blisters and skin sloughing only involving sun-exposed skin within hours of exposure, with resolution within days of discontinuation of the medication. Subsequent photopatch testing confirmed the diagnosis.

3.1.6 Antiretrovirals

A variety of photosensitive eruptions have been reported to occur in patients with HIV, including polymorphous light eruption, porphyria cutanea tarda, actinic prurigo and chronic actinic dermatitis, photosensitive granuloma annulare and lichenoid photoeruption. These reactions can occur in the setting of HIV, independent of any medications [101, 102]. As such, elucidating the role of antiretrovirals in HIV-associated photodermatoses can be challenging.

Efavirenz is a non-nucleoside reverse transcriptase inhibitor used in the treatment of HIV infection. Efavirenz-induced photosensitivity has been reported [103–106] and confirmed by photopatch testing, evidence that efavirenz, and perhaps other antiretroviral medications, may be the culprit in some cases of photosensitivity associated with HIV. Other reports have suggested the possible association between antiretroviral therapy and other photo-induced reactions, including a porphyria cutanea tarda-like blistering eruption [107], although these reports lack photopatch testing or rechallenge evidence. Tenofovir has also been confirmed to cause a photosensitive eruption in a single patient as confirmed by histopathology and photopatch testing [108].

3.2 Non-Steroidal Anti-Inflammatory Drugs

The non-steroidal anti-inflammatory drugs (NSAIDs) are a heterogenous class of medications that act by inhibiting prostaglandin synthesis and are used for a variety of symptoms including pain, inflammation and fever. Photosensitivity has been reported with a number of NSAIDs. Historically, photosensitivity was reported most commonly with benoxaprofen and piroxicam [109, 110]. In the past, it was reported that over 50% of the adverse reactions associated with benoxaprofen were photosensitive and often severe. In one patient, histologic examination of a biopsy from a sun-exposed area showed deep cutaneous injury with prominent

sweat gland necrosis. Because of the adverse effects associated with its use, benoxaprofen was withdrawn from the market in the early 1980s. Piroxicam, which is still available on the market, has been reported to cause photosensitivity including vesiculobullous, eczematous and lichenoid reactions [110–112].

Among commonly used NSAIDs, naproxen appears to have the most photosensitizing potential. Patients most often present with pseudoporphyria [113–115], although more typical phototoxic reactions, as well as erythema multiforme and lichenoid eruptions, have also been reported [109, 116, 117]. Multiple reports comment on similar phototoxic reactions with oxaprozin [114, 118], nabumetone [114, 119], ampiroxicam [120], tiaprofenic acid [109], sulindac [110] and meclofenamide sodium [110]. Diclofenac, although not reported to cause skin eruptions, has been reported to cause photo-onycolysis [121]. Ibuprofen is not considered to be a potent photosensitizer, and to date, only one case report documenting a photosensitive reaction in a patient on this medication has been reported [122]. Interestingly, subsequent testing found this patient to have a decreased MED to the UVA spectrum while taking ibuprofen; however, photopatch testing was negative. Celecoxib, a cyclooxygenase 2 inhibitor, has also been reported to cause photoallergic reactions and pseudoporphyria [113, 123, 124]. Photopatch testing was carried out in one patient but again was negative.

A recent study found an increased risk of cutaneous melanoma in those taking NSAIDs, and it has been proposed that this is related to their phototoxic potential [55]. However, results in the literature are mixed, including some studies that have found protective effects of NSAIDs on skin cancer risk; in a systematic review and meta-analysis, no association was seen between NSAID use and melanoma [125].

Table 4 NSAIDs reported to cause photosensitive drug eruptions

Drug	Evidence
Piroxicam	PP [112]
Naproxen	PP [117], PT [92]
Oxaprozin	–
Nabumetone	–
Ampiroxicam	PP [120]
Tiaprofenic acid	–
Sulindac	–
Meclofenamide sodium	–
Diclofenac	–
Indomethacin	PP [110], RC [110]
Ibuprofen	RC [122]
Celecoxib	–

PP photopatch testing, *PT* phototesting, *RC* rechallenge, – indicates test not done or test negative

3.3 Antihypertensives

3.3.1 Diuretics

Thiazides are some of the most commonly prescribed diuretics, first coming to market in the 1950s. Shortly after their introduction, reports of photosensitivity reactions were documented. The most commonly reported culprit is hydrochlorothiazide, with over 60 cases published to date [126] including exaggerated sunburn reactions, eczematous lesions in a photodistributed pattern, lichenoid eruptions and photoleukomelanoderma [4, 127, 128]. Importantly, chronic eczematous photosensitivity has been reported lasting months to years after discontinuation of the drug [129]. Such patients have been successfully treated with PUVA. In some of the reports, photobiological studies were included, suggesting that thiazide photosensitivity can be elicited by both UVA and UVB. Positive photopatch testing to hydrochlorothiazide has been reported, and in some cases the results of phototesting were normal with only photopatch testing yielding abnormal results [126, 130].

Indapamide, a thiazide-like diuretic, has not been reported to cause cutaneous phototoxicity reactions, although photo-onycholysis has been described [131]. Phototesting and photopatch results have been negative.

Table 5 Antihypertensive medications reported to cause photosensitive drug eruptions

Subclass	Drug	Evidence
Diuretics	Thiazides	PP [130], PT [4, 129]
	Furosemide	RC [133]
	Indapamide	–
	Triamterene	PP [135], RC [135]
ACE inhibitors	Ramipril	PP [138]
	Enalapril	–
	Quinapril	PT [137], RC [137]
Angiotensin receptor blockers	Valsartan	–
	Olmesartan	RC [141]
	Losartan	–
	Irbesartan	–
	Valsartan	–
	Candesartan	–
	Telmisartan	–
Calcium channel blockers	Amlodipine	PT [143]
	Nifedipine	RC [146]
	Diltiazem	PT [148], RC [149]
Beta blockers	Tilisolol	PP [150], RC [150]
Centrally acting agents	Rilmenidine	PT [151]
	Methyldopa	PP [152]

PP photopatch testing, *PT* phototesting, *RC* rechallenge, – indicates test not done or test negative

Furosemide, another popular diuretic, has also been linked to phototoxic eruptions. Unlike the thiazides, furosemide-associated photosensitivity typically presents with bullous eruptions, some mimicking a Brunsting–Perry–type presentation of localized bullous pemphigoid [132–134]. In one study, rechallenge testing was positive [133].

Other less commonly prescribed diuretics, including triamterene, a potassium sparing diuretic, have been reported to cause photosensitivity with positive photopatch testing [135].

3.3.2 ACE Inhibitors and Angiotensin Receptor Blockers

The ACE inhibitors (ACEi) and angiotensin receptor blockers (ARBs) are two groups of closely related anti-hypertensive medications that work primarily on the renin-angiotensin-aldosterone pathway. They are commonly used in the management of hypertension, renal failure and heart failure. Among the ACEi, ramipril, quinapril and enalapril have been reported to cause photosensitivity, with positive photopatch testing results for ramipril and rechallenge evidence for quinapril [136–139].

There are few reports in the literature of ARB-induced photosensitivity [140, 141]. However, a recent review of VigiBase, a global WHO database of individual case safety reports, identified numerous cases of probable or possible photosensitivity reactions to ARBs between 1968 and 2014 [141]. Most commonly, these reactions occurred with losartan, irbesartan and valsartan, and up to 10% have been reported as serious. Other less common culprits include olmesartan, candesartan and telmisartan. Positive rechallenge has been documented for olmesartan [141].

3.3.3 Calcium Channel Blockers

Amlodipine and nifedipine are calcium channel blockers (CCBs) in the dihydropyridine group that have been reported to cause photodistributed facial telangiectasia, a distinct photo-induced morphology, and may cross-react with each other in causing this phenomenon [142–145]. Nifedipine has also been reported to cause a photodermatitis, confirmed by rechallenge. Photopatch testing carried out on one of two patients was negative [146].

Diltiazem, a benzothiazepine CCB, has been implicated as a cause of photodistributed hyperpigmentation [147, 148]. It has also been reported to cause photosensitive dermatitis, proven by rechallenge [149].

3.3.4 Other Antihypertensive Agents

The beta blocker (β-blocker) tilisolol has been reported to cause photosensitivity in a single patient with confirmation by rechallenge and photopatch testing [150]. To our knowledge, it is the only β-blocker that has been reported to cause photosensitivity.

Rilmenidine, a central imidazoline agonist, has been reported to cause erythema and swelling in a photodistributed pattern, again in only one patient [151].

Methyldopa, another centrally acting antihypertensive, may cause photosensitivity. A positive photopatch test response was documented in one patient [152].

Several recent studies have identified positive associations between the use of antihypertensives and the risk of cutaneous malignancy. For instance, a recent study has found an increased risk of both squamous cell carcinoma and cutaneous melanoma in people taking amiloride and hydrochlorothiazide combination therapy, and an increased risk of cutaneous melanoma in those taking indapamide [5]. It has been proposed that this is related to the phototoxic potential of these medications. A recent meta-analysis looking at the association between anti-hypertensive drugs and skin cancer risk identified that users of CCBs and β-blockers were at increased risk of skin cancer and cutaneous melanoma, respectively. However, even when positive, associations were weak. The authors identified no association between thiazide diuretics, ACEi or ARB use and skin cancer risk [153]. Additional studies are required.

3.4 Antiarrhythmics

Amiodarone is a potent class III antiarrhythmic used to prevent and treat ventricular arrhythmias and atrial fibrillation. It has a number of potential side effects including photosensitivity. In some studies, phototoxicity was seen in over 50% of patients taking amiodarone [154–156], although more recent studies suggest it occurs in closer to 7% of patients [157]. Amiodarone photosensitivity classically presents with a burning/tingling sensation in sun-exposed skin followed by the development of erythema and eczema; however, pseudoporphyria reactions have also been reported. Particularly after long-term exposure, amiodarone induces a distinctive blue-grey pigmentation on sun-exposed sites in 1–2% of patients [155, 158]. The photosensitivity usually resolves within months of discontinuation of the drug; however, persistent reactions have also been reported [159]. Photo-induced pigmentation generally fades gradually over 1–2 years [160]. UVA and UVB are both involved in amiodarone-induced photosensitivity [158, 161]. Dronedarone, a novel antiarrhythmic that is similar in composition to amiodarone, appears to be significantly less phototoxic than amiodarone. However, cases of photosensitivity have been reported [162].

Quinidine, a class I antiarrhythmic, has also been reported to cause photosensitivity presenting as an eczematous dermatitis, a lichenoid eruption or a livedoid purpuric eruption [163–165]. In one report, the histology and clinical

Table 6 Antiarrhythmic medications reported to cause photosensitive drug eruptions

Drug	Evidence
Amiodarone	PT [158, 161]
Dronedarone	–
Quinine and quinidine	See Table 3
Calcium channel blockers	See Table 5

PT phototesting, – indicates test not done or test negative

presentation were consistent with a photoallergic reaction [164]. The diagnosis was confirmed in one study by phototesting and rechallenge, and in another by photopatch testing [163, 166].

Other antiarrhythmics that cause photosensitivity, the calcium channel blockers and quinine, are discussed in earlier sections of this paper.

3.5 Cholesterol-Lowering Agents

The HMG-CoA reductase inhibitors (statins) are the most commonly prescribed lipid-lowering agents worldwide. They have been reported to cause photosensitivity, but this is not a common adverse effect of this class of medications. Simvastatin may cause a persistent photodistributed dermatitis [167, 168]. Photopatch testing and rechallenge with phototesting have both been positive for simvastatin [167, 169]. Atorvastatin has been reported to cause an edematous erythema on sun-exposed sites, proven by rechallenge [170]. Its phototoxic potential is thought to arise from singlet oxygen generation via a phenanthrene-like photoproduct [171]. Both simvastatin and pravastatin have been reported to cause photodistributed erythema multiforme [172].

Fenofibrate is a lipid-lowering agent that works by a distinct mechanism. It has been reported to cause eczematous and lichenoid photosensitivity, proven by both photopatch testing and rechallenge [173–176].

Table 7 Cholesterol-lowering medications reported to cause photosensitive drug eruptions

Subclass	Drug	Evidence
HMG-CoA reductase inhibitors (statins)	Simvastatin	PT [169, 172], PP [167, 169], RC [167]
	Atorvastatin	PT [170], RC [170]
	Pravastatin	PT [172]
Fibrates	Fenofibrate	PT [175], PP [175], RC [175]

PP photopatch testing, *PT* phototesting, *RC* rechallenge

3.6 Chemotherapeutics

3.6.1 Antimetabolite Therapies

Fluorouracil and several related compounds have been reported to cause photosensitive eruptions. Fluorouracil can cause enhanced sunburn reactions, photodistributed hyperpigmentation or polymorphous light eruption-like reactions [177]. Tegafur, a fluorouracil derivative, may cause both lichenoid and eczematous photodistributed reactions [178–180]. Rechallenge, as well as photopatch testing, has been positive, with photopatch testing being positive in only those cases where the reaction was eczematous. Capecitabine, a fluorouracil pro-drug, has been reported to cause photodistributed lichenoid eruptions [181–184]. Capecitabine may be less photosensitizing than fluorouracil and may be an alternative treatment for patients unable to tolerate fluorouracil-induced photosensitivity [185].

Dacarbazine, also known as imidazole carboxamide, is a chemotherapeutic agent used in the treatment of melanoma and Hodgkin's lymphoma. It acts by methylating guanine nucleotides and disrupting DNA synthesis. Photosensitive eruptions to dacarbazine have been reported and rechallenge evidence exists [186–189]. In one study, participants displaying photosensitivity to dacarbazine, with increased UVA-sensitivity, were switched to temozolomide without reaction. It is suggested that temozolomide may be used as an alternative to dacarbazine in patients who do not tolerate this medication due to photosensitivity [190].

Table 8 Chemotherapeutic medications reported to cause photosensitive drug eruptions

Subclass	Drug	Evidence
Antimetabolites	Fluorouracil	–
	Tegafur	PT [178], PP [179], RC [178, 180]
	Capecitabine	–
	Dacarbazine	PT [189, 190], RC [189]
Antimitotic agents	Taxanes	–
	Doxorubicin	–
	Epirubicin	PP [194]
	Vinblastine	RC [195]
Targeted therapies	Vemurafenib	PT [196]
	Vandetanib	PT [200]
	Erlotinib	–
	Crizotinib	RC [203]
	Imatinib	RC [205, 206]
Miscellaneous agents	Hydroxyurea	–
	Flutamide	PP [210], RC [211]
	Bicalutamide	PT [212]

PP photopatch testing, *PT* phototesting, *RC* rechallenge, – indicates test not done or test negative

3.6.2 Antimitotic Agents

The taxanes are a class of antineoplastic agents that disrupt microtubule function and cell division. They are commonly used in the treatment of breast, lung and head and neck carcinomas. Perhaps the best-known member of this class, paclitaxel, has been reported to cause photodistributed erythema multiforme as well as onycholysis [191, 192]. More recently, photosensitive reactions have also been reported for the nanoparticle albumin–bound paclitaxel derivative (nab-paclitaxel) [193]. Other well known agents in this class, including doxorubicin, are also reported to cause photosensitivity reactions. Additionally, photopatch testing was positive in a patient with a bullous eruption secondary to epirubicin [194].

Vinblastine, originally derived from the periwinkle plant, is an anti-mitotic agent used in the treatment of many malignancies, most commonly Hodgkin's lymphoma. Vinblastine has been reported to cause photosensitivity reactions. As well, there is rechallenge evidence for vinblastine phototoxicity in a patient who developed a photodistributed vesicular eruption while on the drug [195]. To our knowledge, vincristine, a chemical analogue of vinblastine, has not been reported to cause photosensitivity reactions.

3.6.3 Targeted Therapies

Vemurafenib, a BRAF inhibitor indicated in the treatment of late stage melanoma, is one of the most common culprits associated with photosensitivity reactions. In a recent review of 520 patients evaluating the cutaneous side effects of this anti-cancer therapy, photosensitivity was reported in 35–63% of patients [7]. Studies have confirmed the photosensitivity of vemurafenib through phototesting with UVA [196]. Importantly, while vemurafenib may induce cutaneous squamous cell carcinomas, these do not appear related to vemurafenib-induced phototoxicity [7].

Vandetanib, a tyrosine kinase inhibitor, has been associated with the development of a photodistributed erythematous, vesiculobullous eruption in patients being treated for thyroid [197], lung [198] and hepatocellular carcinoma [199]. Erythema multiforme-like lesions have also been reported in a single patient treated with vandetanib for thyroid carcinoma [200]. Additionally, several patients have been noted to develop pigmentation in photo-exposed sites (in addition to other locations e.g. scars) while taking this medication [201]. Another tyrosine kinase inhibitor targeting the epidermal growth factor receptor, erlotinib, has also recently been reported to cause photosensitivity [202]. Crizotinib, a tyrosine kinase inhibitor targeting anaplastic lymphoma kinase, has been confirmed to cause phototoxicity, supported by rechallenge evidence [203].

Imatinib, another drug in this class targeting BCR-ABL, has been reported to cause exaggerated sunburn reactions, photo-induced dermatitis and pseudoporphyria in patients being treated for chronic myelogenous leukemia [204–206]. In one report, the dermatitis was noted to resolve with withdrawal of the medication and recur upon rechallenge [205].

3.6.4 Other Chemotherapeutics

Several other chemotherapeutic agents have been reported to cause photosensitivity reactions. Hydroxyurea has been reported to cause a photodistributed dermatitis in a patient with chronic myeloid leukemia [207] and, in another patient, a photodistributed granulomatous rash was noted [208]. Flutamide and bicalutamide, used in the treatment of prostate cancer, have been reported to cause photosensitivity. With flutamide, there is documented photopatch and rechallenge positivity [209–211] and with bicalutamide, photosensitivity was confirmed by phototesting [212, 213].

3.7 Psychotropic Medications

3.7.1 Antipsychotics

The phenothiazine antipsychotics, chlorpromazine and thioridazine, have both been reported to cause photosensitivity [214–216]. Reported reactions to chlorpromazine include exaggerated sunburn reactions, lichenoid reactions and bullous eruptions [217–219]. Patients taking both thioridazine and chlorpromazine have had positive photopatch responses to these drugs [215, 218, 219]. Long-term, high-dose therapy with either chlorpromazine or thioridazine can result in photodistributed slate-grey to violaceous hyperpigmentation [216]. Flupenthixol, an antipsychotic drug structurally related to the phenothiazines, has also been reported to cause photosensitivity; however, photopatch testing was negative [220]. Haloperidol has been reported to cause a photosensitive dermatitis in one patient [221]. Although the atypical antipsychotics are felt to be less photosensitizing, reactions have been reported. Olanzapine has been reported to cause photo-onycholysis, which was further exacerbated after switching to aripiprazole [222]. Photosensitivity to clozapine [223, 224] and risperidone [225] has been documented.

Table 9 Psychotropic medications reported to cause photosensitive drug eruptions

Subclass	Drug	Evidence
Antipsychotics	Chlorpromazine	PT [217], PP [218, 219]
	Thioridazine	PP [215]
	Flupenthixol	Photoprick testing [220]
	Haloperidol	–
	Olanzapine	–
	Clozapine	–
	Aripiprazole	–
	Risperidone	–
Antidepressants	Imipramine	–
	Clomipramine	PP [229], RC [229]
	Escitalopram	–
	Citalopram	–
	Paroxetine	PT [234], PP [231, 232]
	Fluoxetine	–
	Fluvoxamine	PP [231, 233]
	Sertraline	–
	Venlafaxine	PT [239]
	Phenelzine	–
Anxiolytics	Alprazolam	PT [242], RC [242]
	Chlordiazepoxide	RC [243]

PP photopatch testing, *PT* phototesting, *RC* rechallenge, – indicates test not done or test negative

3.7.2 Antidepressants

The tricyclic antidepressants, which are chemically related to the phenothiazines, have been reported to cause photosensitivity. Imipramine caused a photodistributed erythema, as well as a blue-grey hyperpigmentation in photodistributed areas following long-term use [226–228]. Clomipramine has been implicated as a cause of photoallergy, with photopatch and rechallenge testing having been performed [229].

The most commonly prescribed antidepressant medications, the selective serotonin reuptake inhibitors (SSRIs), have been reported to cause photosensitivity reactions. In their report of erythroderma on sun-exposed sites following artificial tanning while taking escitalopram, Ram-Wolf et al. reviewed all of the reported cases of SSRI photosensitivity in the literature to that point [230]. Since that time, several new reports have emerged implicating even more SSRIs in photosensitivity eruptions. Paroxetine [231, 232] and fluvoxamine [231, 233] have both demonstrated photosensitivity with photopatch positivity. In one patient treated with paroxetine, this manifested as photodistributed granuloma annulare with confirmation via phototesting [234]. Additionally, sertraline has been implicated as the cause of a macular erythematous photoallergic reaction [235]. Fluoxetine has been reported to cause photosensitive reactions, including erythema and blisters [236, 237], and citalopram has been implicated in photodistributed hyperpigmentation [238]. Venlafaxine, a serotonin-noradrenaline reuptake inhibitor (SNRI), has been reported to cause photodistributed telangiectasia [239]. There are no reports to our knowledge of other SNRI medications, namely duloxetine or desvenlafaxine, causing photosensitivity. The monoamine oxidase inhibitor phenelzine has been reported to cause clinical photosensitivity [240].

3.7.3 Anxiolytics

Alprazolam, a benzodiazepine anxiolytic, has been reported to cause pruritic erythema in sun-exposed sites, with photosensitivity confirmed by rechallenge [237, 241, 242]. Chlordiazepoxide has also been implicated as a cause of a photo-induced eczematous eruption [243].

3.8 Miscellaneous Medications

3.8.1 Hormone Contraceptives

Several case reports have documented photosensitive eruptions following the use of combined oral contraceptives containing either ethinylestradiol and levonorgestrel [244] or ethinylestradiol and desogestrel, with recurrence of this eruption on rechallenge with a second pill containing ethinylestradiol and levonorgestrel [245]. Similar reactions have also been reported with the use of a contraceptive patch containing norelgestromin and ethinylestradiol, with recurrence of the erythematous, vesicular eruption when the patient was switched to an oral contraceptive pill containing ethinylestradiol and drospirenone. The report concluded that ethinylestradiol was most likely the offending agent. Rechallenge testing with the oral contraceptive pill was positive [246].

3.8.2 Systemic Retinoids

Systemic retinoids are often implicated as a cause of photosensitivity. However, evidence supporting this claim is lacking. Ferguson and Johnson addressed this question through a literature review and experimental testing with both etretinate and isotretinoin [247, 248]. Clinical and experimental evidence supporting etretinate-induced photosensitivity was demonstrated, but no clinical or experimental evidence was found to suggest isotretinoin-induced photosensitivity. Another study reported similar results for isotretinoin [249]. Etretinate-induced photosensitivity typically manifests as increased susceptibility to sunburn, although pseudoporphyria [250] and photoleukomelanoderma [251] have also been reported. To our knowledge, there have been no

Table 10 Miscellaneous medications reported to cause photosensitivity drug eruptions

Class	Drug	Evidence
Retinoids	Etretinate	PT [247, 248], PP [251], RC [251]
	Isotretinoin	–
Contraceptive hormones	Ethinylestradiol	RC [245, 246]
Antihistamines	Ranitidine	RC [256, 257]
	Diphenhydramine	PP [252, 253]
	Mequitazine	PP [254]
	Repirinast	PT [255], RC [255]
Anticonvulsants	Carbamazepine	PP [262, 263], RC [263]
Oral hypoglycemic agents	Glibenclamide (glyburide)	PT [260]
	Sitagliptin	–
	Metformin	RC [258]
Antiplatelet agents	Clopidogrel	RC [265]
	Triflusal	PT [266]
Proton pump inhibitors	Pantoprazole	–
	Esomeprazole	–
Monoclonal antibody	Eculizumab	–
	Tocilizumab	–
Anti-inflammatory	Leflunomide	–
	Mesalazine	–
Others	Pirfenidone	–
	2-Mercaptoethane sulfonate sodium (Mesna)	–

PP photopatch testing, *PT* phototesting, *RC* rechallenge, – indicates test not done or test negative

recent reports documenting a confirmed case of isotretinoin-induced photosensitivity.

3.8.3 Antihistamines

Diphenhydramine, one of the most commonly used antihistamines, has been reported to cause photosensitivity, confirmed through photopatch testing [252, 253]. The phenothiazine antihistamine mequitazine has been demonstrated to be photosensitizing, with positive photopatch results [254]. Repirinast has been reported to cause solar urticaria [255]. Ranitidine, an antihistamine used to treat gastroesophageal reflux disease, has been reported to cause a papulosquamous eruption on sun-exposed sites confirmed by rechallenge [256]. A second case report of ranitidine-induced photosensitivity was confirmed through normalization of the patient's phototest results on discontinuation of the medication [257].

3.8.4 Diabetes Medications

Metformin, a medication commonly used in the management of diabetes mellitus as well as other conditions, has been linked to the development of both erythematous and eczematous photosensitivity eruptions in three patients, one of which was confirmed with positive rechallenge evidence [258]. Glibenclamide (glyburide), a sulfonylurea oral hypoglycaemic agent, has been reported to cause an eczematous photodermatitis [259, 260]. While phototesting has revealed increased sensitivity to UVA and UVB with glibenclamide, photopatch testing has been negative and rechallenge testing has not been performed [260]. Sitagliptin, a dipeptidyl peptidase-4 inhibitor, has also been reported to cause a prolonged photosensitive eruption in a single patient [261].

3.8.5 Others

Carbamazepine has been reported to cause both photosensitive eczematous and lichenoid eruptions, with photopatch and rechallenge evidence [262, 263]. An unusual reaction was reported where carbamazepine-induced facial burns occurred in one patient secondary to prolonged use of a photocopier [264]. Clopidogrel, an antiplatelet agent, has been reported to cause a lichenoid photodistributed eruption, confirmed by rechallenge [265]. The platelet aggregation inhibitor, triflusal, has also been reported to cause an extensive, eczematous photodistributed eruption in a single patient [266]. Pirfenidone, a medication used in the treatment of idiopathic pulmonary fibrosis, has recently been implicated in photosensitivity reactions ranging from exfoliative erythema [267] to photoleukomelanoderma [268].

Although not typically considered to be photosensitizing, case reports of proton pump inhibitor-induced photosensitivity have been published for both pantoprazole [269] and esomeprazole [270]. Importantly, in the case of esomeprazole-induced photosensitive dermatitis, the reactions resolved on discontinuation of the drug and did not recur when the patient was initiated on ranitidine, suggesting little potential for cross-reactivity between these different classes of medications.

Eculizumab, leflunomide, mesalazine, tocilizumab and 2-mercaptoethane sulfonate sodium (Mesna) have all been reported to cause photosensitivity, but none, to the best of our knowledge, have been evaluated by phototesting or photopatch testing [271–275].

4 Prevention and Management

Physicians should be aware of the photosensitizing potential of the medications they prescribe, particularly for those with well documented evidence (e.g. tetracycline antibiotics, amiodarone), and should counsel patients about sun avoidance and sun protection when initiating treatment with a known photosensitizing medication. The tables provided in this document provide a framework for understanding which medications have been reported to cause photosensitivity; however, not all of these have high quality evidence to support their photosensitizing potential, and photosensitivity from most of the listed medications is not common. Medications that are considered potent photosensitizers are listed in Table 2, and these warrant physician and patient awareness prior to their prescription.

Should a patient present with a new rash when taking a potentially photosensitizing medication, the physician's first goal should be to obtain a thorough history, particularly focusing on the chronology of medication in relation to the onset of the cutaneous eruption. Along with the history, physical examination will help to determine if the rash is photo-induced. Physical examination generally reveals a photodistributed pattern to the eruption with sparing of photo-protected sites (e.g. upper eyelids, bases of folds including the nasolabial folds, and the submental and posterior auricular regions). Of note, one must be cautious about distinguishing true photosensitivity from photorecall reactions, a reaction that is most commonly associated with chemotherapeutic agents. In a photorecall reaction, drug administration even in the absence of sunlight triggers a sunburn-like reaction in the same distribution of a prior sunburn the patient acquired months to years earlier. This photorecall reaction has been most commonly reported with methotrexate but has also been described with gemcitabine and the taxanes [276–281].

If a drug-induced photosensitive eruption is suspected, diagnostic tests, including phototesting, photopatch testing and clinical rechallenge (with possible repeating phototesting) may be carried out to help clarify the diagnosis and the culprit medication. While these tests are not always available or necessary, phototesting may be useful in assessing for other causes of photosensitivity where the situation is clinically unclear. Repeat phototesting several months after discontinuation of the suspected drug can also help clarify that the cause of photosensitivity is a drug reaction. Once a diagnosis of a drug-induced photosensitivity disorder is made and the offending drug is identified, the most important aspect of management is discontinuation of the drug [282]. While persistent photosensitivity may occur, the photosensitivity usually abates shortly after the photosensitizing medication is discontinued. In some cases, photosensitivity persists for several months despite discontinuation of the medication. As such, it is recommended that repeat phototesting only occur 3–6 months following discontinuation of the offending agent.

Discontinuation of the photosensitizing medication may not be possible for all patients. When this is the case, secondary prevention measures such as sun avoidance, especially during peak daylight hours, and the use of sun protective clothing and sunscreens with both UVA and UVB protection should be implemented. Other strategies that have been reported include administering medications in the evening [283], although the effectiveness of this strategy would be highly dependent on the pharmacokinetic properties of the medication. Alternatively, 'hardening' with gradually increasing doses of narrowband UVB phototherapy has been reported as a viable strategy to increase tolerance to sun exposure for a patient with amiodarone-induced photosensitivity [284].

For patients who are symptomatic, the use of topical or systemic corticosteroids may be helpful to treat drug-induced photosensitive eruptions. This is helpful to hasten resolution of the photo-induced eruption as the culprit medication is being discontinued. Topical corticosteroids can also be used when a photosensitizing agent cannot be discontinued. Early treatment of the eruption is advisable as one study regarding sparfloxacin photosensitivity found that delayed treatment of photosensitive eruptions may make them more difficult to treat [285].

5 Conclusion

The exact incidence of drug-induced photosensitivity is unknown, but for some medications it is quite common. The diagnosis of photo-induced drug eruptions is largely clinical but can be assisted by diagnostic tests such as phototesting, photopatch testing and rechallenge testing. A large number of medications have been implicated in the literature as causes

of photosensitivity, many with convincing clinical and scientific support. This comprehensive narrative review has been assembled to help direct both the physician and patient as to common culprits of drug-induced photosensitivity reactions. This review helps to build on a growing compendium of information on this topic, but also provides the added benefit of detailed discussion regarding the reported clinical manifestations for each reported reaction as well as a dissection of the explicit clinical testing completed to confirm each culprit medication. This resource will help to guide physicians starting potentially photosensitizing medications, as well as those faced with evaluating potential drug-induced rashes. It is important for clinicians to recognize these eruptions, regardless of the causative agent, and treat them accordingly. For medications that are known to be potent photosensitizers, patient education regarding this potential side effect prior to initiation of therapy is imperative.

Compliance with Ethical Standards

Conflict of interest Kim M. Blakely, Aaron M. Drucker and Cheryl F. Rosen have no conflicts of interest that are directly related to the content of this study. Outside of this work, Aaron M. Drucker has served as an investigator and has received research funding from Sanofi and Regeneron and has been a consultant for Sanofi, RTI Health Solutions, Eczema Society of Canada and Canadian Agency for Drugs and Technology in Health. He has received honoraria from Prime Inc, Spire Learning, CME Outfitters and Eczema Society of Canada. His institution has received educational grants from Sanofi. Outside of this work, Cheryl F. Rosen has served as a consultant for AbbVie Corporation, Janssen Inc. and Novartis Pharmaceuticals. She also receives research support from AbbVie and Janssen. Her institution has received educational grants from Bausch, Celgene, AbbVie and Janssen.

Funding No sources of funding were used to assist in the preparation of this study.

References

1. Selvaag E. Clinical drug photosensitivity. A retrospective analysis of reports to the Norwegian Adverse Drug Reactions Committee from the years 1970–1994. Photodermatol Photoimmunol Photomed. 1997;13(1–2):21–3.
2. Mang R, Stege H, Krutmann J. Mechanisms of phototoxic and photoallergic reactions. In: Johansen J, Frosch P, Lepoittevin JP, editors. Contact dermatitis. Berlin: Springer; 2011.
3. Willis I, Kligman AM. The mechanism of photoallergic contact dermatitis. J Investig Dermatol. 1968;51(5):378–84.
4. Addo HA, Ferguson J, Frain-Bell W. Thiazide-induced photosensitivity: a study of 33 subjects. Br J Dermatol. 1987;116(6):749–60.
5. Jensen AO, Thomsen HF, Engebjerg MC, Olesen AB, Sorensen HT, Karagas MR. Use of photosensitising diuretics and risk of skin cancer: a population-based case-control study. Br J Cancer. 2008;99(9):1522–8. https://doi.org/10.1038/sj.bjc.6604686.
6. Kolaitis NA, Duffy E, Zhang A, Lo M, Barba DT, Chen M, et al. Voriconazole increases the risk for cutaneous squamous cell carcinoma after lung transplantation. Transpl Int. 2017;30(1):41–8. https://doi.org/10.1111/tri.12865.
7. Lacouture ME, Duvic M, Hauschild A, Prieto VG, Robert C, Schadendorf D, et al. Analysis of dermatologic events in vemurafenib-treated patients with melanoma. Oncologist. 2013;18(3):314–22. https://doi.org/10.1634/theoncologist.2012-0333.
8. Miller DD, Cowen EW, Nguyen JC, McCalmont TH, Fox LP. Melanoma associated with long-term voriconazole therapy: a new manifestation of chronic photosensitivity. Arch Dermatol. 2010;146(3):300–4. https://doi.org/10.1001/archdermatol.2009.362.
9. Williams K, Mansh M, Chin-Hong P, Singer J, Arron ST. Voriconazole-associated cutaneous malignancy: a literature review on photocarcinogenesis in organ transplant recipients. Clin Infect Dis. 2014;58(7):997–1002. https://doi.org/10.1093/cid/cit940.
10. Drucker AM, Rosen CF. Drug-induced photosensitivity: culprit drugs, management and prevention. Drug Saf. 2011;34(10):821–37. https://doi.org/10.2165/11592780-000000000-00000.
11. Spielmann H, Balls M, Brand M, Doring B, Holzhutter HG, Kalweit S, et al. EEC/COLIPA project on in vitro phototoxicity testing: first results obtained with a Balb/c 3T3 cell phototoxicity assay. Toxicol In Vitro. 1994;8(4):793–6.
12. Spielmann H, Muller L, Averbeck D, Balls M, Brendler-Schwaab S, Castell JV, et al. The second ECVAM workshop on phototoxicity testing. The report and recommendations of ECVAM workshop 42. Altern Lab Anim. 2000;28(6):777–814.
13. Traynor NJ, Barratt MD, Lovell WW, Ferguson J, Gibbs NK. Comparison of an in vitro cellular phototoxicity model against controlled clinical trials of fluoroquinolone skin phototoxicity. Toxicol In Vitro. 2000;14(3):275–83.
14. Kerr A, Shareef M, Dawe R, Ferguson J. Photopatch testing negative in systemic quinine phototoxicity. Photodermatol Photoimmunol Photomed. 2010;26(3):151–2. https://doi.org/10.1111/j.1600-0781.2010.00503.x.
15. Conilleau V, Dompmartin A, Michel M, Verneuil L, Leroy D. Photoscratch testing in systemic drug-induced photosensitivity. Photodermatol Photoimmunol Photomed. 2000;16(2):62–6.
16. Kim WB, Shelley AJ, Novice K, Joo J, Lim HW, Glassman SJ. Drug-induced phototoxicity: a systematic review. J Am Acad Dermatol. 2018. https://doi.org/10.1016/j.jaad.2018.06.061.
17. Goetze S, Hiernickel C, Elsner P. Phototoxicity of doxycycline: a systematic review on clinical manifestations, frequency, cofactors, and prevention. Skin Pharmacol Physiol. 2017;30(2):76–80. https://doi.org/10.1159/000458761.
18. Tanaka N, Kawada A, Ohnishi Y, Hiruma M, Tajima S, Akiyama M, et al. Photosensitivity due to doxycycline hydrochloride with an unusual flare. Contact Dermatitis. 1997;37(2):93–4.
19. Yap LM, Foley PA, Crouch RB, Baker CS. Drug-induced solar urticaria due to tetracycline. Australas J Dermatol. 2000;41(3):181–4.
20. Lim DS, Triscott J. O'Brien's actinic granuloma in association with prolonged doxycycline phototoxicity. Australas J Dermatol. 2003;44(1):67–70.
21. Susong J, Carrizales S. Lichenoid photosensitivity: an unusual reaction to doxycycline and an unusual response. Cutis. 2014;93(5):E1–2.
22. Kestel JL Jr. Photo-onycholysis from minocycline. Side effects of minocycline therapy. Cutis. 1981;28(1):53–4.
23. Gventer M, Brunetti VA. Photo-onycholysis secondary to tetracycline. A case report. J Am Podiatr Med Assoc. 1985;75(12):658–60.
24. Ibsen HH, Lasthein Andersen B. Photo-onycholysis due to tetracycline-hydrochloride. Acta Derm Venereol. 1983;63(6):555–7.

25. Lasser AE, Steiner MM. Tetracycline photo-onycholysis. Pediatrics. 1978;61(1):98–9.
26. Badri T, Ben Tekaya N, Cherif F, Ben Osman Dhahri A. Photo-onycholysis: two cases induced by doxycycline. Acta Dermatovenerol Alp Pannonica Adriat. 2004;13(4):135–6.
27. Wlodek C, Narayan S. A reminder about photo-onycholysis induced by tetracycline, and the first report of a case induced by lymecycline. Clin Exp Dermatol. 2014;39(6):746–7. https://doi.org/10.1111/ced.12350.
28. Yong CK, Prendiville J, Peacock DL, Wong LT, Davidson AG. An unusual presentation of doxycycline-induced photosensitivity. Pediatrics. 2000;106(1):E13.
29. Pazzaglia M, Venturi M, Tosti A. Photo-onycholysis caused by an unusual beach game activity: a pediatric case of a side effect caused by doxycycline. Pediatr Dermatol. 2014;31(1):e26–7. https://doi.org/10.1111/pde.12223.
30. Rabar D, Combemale P, Peyron F. Doxycycline-induced photo-onycholysis. J Travel Med. 2004;11(6):386–7.
31. Layton AM, Cunliffe WJ. Phototoxic eruptions due to doxycycline—a dose-related phenomenon. Clin Exp Dermatol. 1993;18(5):425–7.
32. Lim DS, Murphy GM. High-level ultraviolet A photoprotection is needed to prevent doxycycline phototoxicity: lessons learned in East Timor. Br J Dermatol. 2003;149(1):213–4.
33. Li WQ, Drucker AM, Cho E, Laden F, VoPham T, Li S, et al. Tetracycline use and risk of incident skin cancer: a prospective study. Br J Cancer. 2018;118(2):294–8. https://doi.org/10.1038/bjc.2017.378.
34. Birkett DA, Garretts M, Stevenson CJ. Phototoxic bullous eruptions due to nalidixic acid. Br J Dermatol. 1969;81(5):342–4.
35. Burry JN. Letter: Persistent phototoxicity due to nalidixic acid. Arch Dermatol. 1974;109(2):263.
36. Mehlhorn AJ, Brown DA. Safety concerns with fluoroquinolones. Ann Pharmacother. 2007;41(11):1859–66. https://doi.org/10.1345/aph.1K347.
37. Ramsay CA, Obreshkova E. Photosensitivity from nalidixic acid. Br J Dermatol. 1974;91(5):523–8.
38. Boisvert A, Barbeau G. Nalidixic acid-induced photodermatitis after minimal sun exposure. Drug Intell Clin Pharm. 1981;15(2):126–7.
39. Zelickson AS. Phototoxic Reaction with Nalidixic Acid. JAMA. 1964;190:556–7.
40. Arata J, Horio T, Soejima R, Ohara K. Photosensitivity reactions caused by lomefloxacin hydrochloride: a multicenter survey. Antimicrob Agents Chemother. 1998;42(12):3141–5.
41. Domagala JM. Structure-activity and structure-side-effect relationships for the quinolone antibacterials. J Antimicrob Chemother. 1994;33(4):685–706.
42. Hayashi N, Nakata Y, Yazaki A. New findings on the structure-phototoxicity relationship and photostability of fluoroquinolones with various substituents at position 1. Antimicrob Agents Chemother. 2004;48(3):799–803.
43. Oliveira HS, Goncalo M, Figueiredo AC. Photosensitivity to lomefloxacin. A clinical and photobiological study. Photodermatol Photoimmunol Photomed. 2000;16(3):116–20.
44. Sanchez JP, Gogliotti RD, Domagala JM, Gracheck SJ, Huband MD, Sesnie JA, et al. The synthesis, structure-activity, and structure-side effect relationships of a series of 8-alkoxy- and 5-amino-8-alkoxyquinolone antibacterial agents. J Med Chem. 1995;38(22):4478–87.
45. Tokura Y, Iwamoto Y, Mizutani K, Takigawa M. Sparfloxacin phototoxicity: potential photoaugmentation by ultraviolet A and B sources. Arch Dermatol Res. 1996;288(1):45–50.
46. Ferguson J, Johnson BE. Ciprofloxacin-induced photosensitivity: in vitro and in vivo studies. Br J Dermatol. 1990;123(1):9–20.
47. Scheife RT, Cramer WR, Decker EL. Photosensitizing potential of ofloxacin. Int J Dermatol. 1993;32(6):413–6.
48. Man I, Murphy J, Ferguson J. Fluoroquinolone phototoxicity: a comparison of moxifloxacin and lomefloxacin in normal volunteers. J Antimicrob Chemother. 1999;43(Suppl B):77–82.
49. Marutani K, Matsumoto M, Otabe Y, Nagamuta M, Tanaka K, Miyoshi A, et al. Reduced phototoxicity of a fluoroquinolone antibacterial agent with a methoxy group at the 8 position in mice irradiated with long-wavelength UV light. Antimicrob Agents Chemother. 1993;37(10):2217–23.
50. Boccumini LE, Fowler CL, Campbell TA, Puertolas LF, Kaidbey KH. Photoreaction potential of orally administered levofloxacin in healthy subjects. Ann Pharmacother. 2000;34(4):453–8. https://doi.org/10.1345/aph.18134.
51. Tolland JP, Murphy BP, Boyle J, Hall V, McKenna KE, Elborn JS. Ciprofloxacin-induced phototoxicity in an adult cystic fibrosis population. Photodermatol Photoimmunol Photomed. 2012;28(5):258–60. https://doi.org/10.1111/j.1600-0781.2012.00676.x.
52. Sailer E, Kamarachev J, Boehler A, Speich R, Hofer M, Benden C, et al. Persistent photodamage following drug photosensitization in a lung-transplant recipient. Photodermatol Photoimmunol Photomed. 2011;27(4):213–5. https://doi.org/10.1111/j.1600-0781.2011.00591.x.
53. Urbina F, Barrios M, Sudy E. Photolocalized purpura during ciprofloxacin therapy. Photodermatol Photoimmunol Photomed. 2006;22(2):111–2. https://doi.org/10.1111/j.1600-0781.2006.00210.x.
54. Rubegni P, Feci L, Pellegrino M, Fimiani M. Photolocalized purpura during levofloxacin therapy. Photodermatol Photoimmunol Photomed. 2012;28(2):105–7. https://doi.org/10.1111/j.1600-0781.2012.00646.x.
55. Siiskonen SJ, Koomen ER, Visser LE, Herings RM, Guchelaar HJ, Stricker BH, et al. Exposure to phototoxic NSAIDs and quinolones is associated with an increased risk of melanoma. Eur J Clin Pharmacol. 2013;69(7):1437–44. https://doi.org/10.1007/s00228-013-1476-x.
56. Borgia F, Vaccaro M, Guarneri F, Cannavo SP. Photodistributed telangiectasia following use of cefotaxime. Br J Dermatol. 2000;143(3):674–5.
57. Vinks SA, Heijerman HG, de Jonge P, Bakker W. Photosensitivity due to ambulatory intravenous ceftazidime in cystic fibrosis patient. Lancet. 1993;341(8854):1221–2.
58. Dhanapaul S. DDS-induced photosensitivity with reference to six case reports. Lepr Rev. 1989;60(2):147–50.
59. Fumey SM. Dapsone-induced photodermatitis in a patient with leprosy. Z Hautkr. 1988;63(1):53–4.
60. Joseph MS. Photodermatitis provoked by dapsone: a case report. Lepr Rev. 1987;58(4):425–8.
61. Kar BR. Dapsone-induced photosensitivity: a rare clinical presentation. Photodermatol Photoimmunol Photomed. 2008;24(5):270–1. https://doi.org/10.1111/j.1600-0781.2008.00372.x.
62. Stockel S, Meurer M, Wozel G. Dapsone-induced photodermatitis in a patient with linear IgA dermatosis. Eur J Dermatol. 2001;11(1):50–3.
63. De D, Dogra S, Kaur I. Dapsone induced acute photosensitivity dermatitis; a case report and review of literature. Lepr Rev. 2007;78(4):401–4.
64. Chandler MJ. Recurrence of phototoxic skin eruption due to trimethoprim. J Infect Dis. 1986;153(5):1001.
65. Lee AY, Jung SY. Two patients with isoniazid-induced photosensitive lichenoid eruptions confirmed by photopatch test. Photodermatol Photoimmunol Photomed. 1998;14(2):77–8.
66. Katiyar SK, Bihari S, Prakash S. Pyrazinamide-induced phototoxicity: a case report and review of literature. Indian J Dermatol. 2010;55(1):113–5. https://doi.org/10.4103/0019-5154.60368.

67. Willis ZI, Boyd AS, Di Pentima MC. Phototoxicity, pseudoporphyria, and photo-onycholysis due to voriconazole in a pediatric patient with leukemia and invasive aspergillosis. J Pediatric Infect Dis Soc. 2015;4(2):e22–4. https://doi.org/10.1093/jpids/piu065.
68. Auffret N, Janssen F, Chevalier P, Guillemain R, Amrein C, Le Beller C. Voriconazole photosensitivity: 7 cases. Ann Dermatol Venereol. 2006;133(4):330–2.
69. Denning DW, Griffiths CE. Muco-cutaneous retinoid-effects and facial erythema related to the novel triazole antifungal agent voriconazole. Clin Exp Dermatol. 2001;26(8):648–53.
70. Frick MA, Soler-Palacin P, Martin Nalda A, Guarner ME, Nadal CF. Photosensitivity in immunocompromised patients receiving long-term therapy with oral voriconazole. Pediatr Infect Dis J. 2010;29(5):480–1. https://doi.org/10.1097/INF.0b013e3181d60a82.
71. Kwong WT, Hsu S. Pseudoporphyria associated with voriconazole. J Drugs Dermatol. 2007;6(10):1042–4.
72. Malani AN, Aronoff DM. Voriconazole-induced photosensitivity. Clin Med Res. 2008;6(2):83–5. https://doi.org/10.3121/cmr.2008.806.
73. Rubenstein M, Levy ML, Metry D. Voriconazole-induced retinoid-like photosensitivity in children. Pediatr Dermatol. 2004;21(6):675–8. https://doi.org/10.1111/j.0736-8046.2004.21614.x.
74. Haylett AK, Felton S, Denning DW, Rhodes LE. Voriconazole-induced photosensitivity: photobiological assessment of a case series of 12 patients. Br J Dermatol. 2013;168(1):179–85. https://doi.org/10.1111/j.1365-2133.2012.11196.x.
75. Barbosa NS, Wetter DA. Bullous phototoxicity from voriconazole. J Emerg Med. 2014;46(3):e83–4. https://doi.org/10.1016/j.jemermed.2013.09.018.
76. Wong JY, Kuzel P, Mullen J, Lien D, Mahmood M, Conrad C, et al. Cutaneous squamous cell carcinoma in two pediatric lung transplant patients on prolonged voriconazole treatment. Pediatr Transplant. 2014;18(6):E200–7. https://doi.org/10.1111/petr.12320.
77. Li AW, Lalor LE, Bellodi Schmidt F, Luu M. A pediatric case of squamous cell cancer in situ in the setting of sclerodermatous graft-versus-host disease and voriconazole treatment. Pediatr Dermatol. 2018;35(3):e165–9. https://doi.org/10.1111/pde.13473.
78. Alvarez-Fernandez JG, Castano-Suarez E, Cornejo-Navarro P, de la Fuente EG, de Ortiz Frutos FJ, Iglesias-Diez L. Photosensitivity induced by oral itraconazole. J Eur Acad Dermatol Venereol. 2000;14(6):501–3.
79. Hawk JL. Photosensitivity induced by oral itraconazole. J Eur Acad Dermatol Venereol. 2000;14(6):445.
80. Mohamed KN. Severe photodermatitis during ketoconazole therapy. Clin Exp Dermatol. 1988;13(1):54.
81. Vassileva SG, Mateev G, Parish LC. Antimicrobial photosensitive reactions. Arch Intern Med. 1998;158(18):1993–2000.
82. Chang TW. Cold urticaria and photosensitivity due to griseofulvin. JAMA. 1965;193:848–50.
83. Kawabe Y, Mizuno N, Miwa N, Sakakibara S. Photosensitivity induced by griseofulvin. Photodermatology. 1988;5(6):272–4.
84. Rimington C, Morgan PN, Nicholls K, Everall JD, Davies RR. Griseofulvin administration and porphyrin metabolism. A Survey. Lancet. 1963;2(7303):318–22.
85. Targovnik SE, Targovnik JH. Cutaneous drug reactions in porphyrias. Clin Dermatol. 1986;4(1):110–7.
86. Watson CJ, Lynch F, Bossenmaier I, Cardinal R. Griseofulvin and porphyrin metabolism. Special reference to normal fecal porphyrin excretion. Arch Dermatol. 1968;98(5):451–68.
87. Kuo S, Sivamani RK. UVB-sensitive solar urticaria possibly associated with terbinafine. Dermatol Online J. 2014;20(3).
88. Gould JW, Mercurio MG, Elmets CA. Cutaneous photosensitivity diseases induced by exogenous agents. J Am Acad Dermatol. 1995;33(4):551–73 **(quiz 74-6)**.
89. Dawson TA. Quinine lichenoid photosensitivity. Clin Exp Dermatol. 1986;11(6):670–1.
90. Ferguson J, Addo HA, Johnson BE, Frain-Bell W. Quinine induced photosensitivity: clinical and experimental studies. Br J Dermatol. 1987;117(5):631–40.
91. Guzzo C, Kaidbey K. Persistent light reactivity from systemic quinine. Photodermatol Photoimmunol Photomed. 1990;7(4):166–8.
92. Ljunggren B, Sjovall P. Systemic quinine photosensitivity. Arch Dermatol. 1986;122(8):909–11.
93. Tan SV, Berth-Jones J, Burns DA. Lichen planus and photo-onycholysis induced by quinine. Clin Exp Dermatol. 1989;14(4):335.
94. Meyrick Thomas RH, Munro DD. Lichen planus in a photosensitive distribution due to quinine. Clin Exp Dermatol. 1986;11(1):97–101.
95. Ljunggren B, Hindsen M, Isaksson M. Systemic quinine photosensitivity with photoepicutaneous cross-reactivity to quinidine. Contact Dermatitis. 1992;26(1):1–4.
96. Singh G, Fries JF, Williams CA, Zatarain E, Spitz P, Bloch DA. Toxicity profiles of disease modifying antirheumatic drugs in rheumatoid arthritis. J Rheumatol. 1991;18(2):188–94.
97. Metayer I, Balguerie X, Courville P, Lauret P, Joly P. Photodermatosis induced by hydroxychloroquine: 4 cases. Ann Dermatol Venereol. 2001;128(6–7):729–31.
98. Lisi P, Assalve D, Hansel K. Phototoxic and photoallergic dermatitis caused by hydroxychloroquine. Contact Dermatitis. 2004;50(4):255–6. https://doi.org/10.1111/j.0105-1873.2004.0301e.x.
99. van Weelden H, Bolling HH, de la Baart H, van der Leun JC. Photosensitivity caused by chloroquine. Arch Dermatol. 1982;118(5):290.
100. Amelot A, Dupouy-Camet J, Jeanmougin M. Phototoxic reaction associated with Malarone (atovaquone/proguanil) antimalarial prophylaxis. J Dermatol. 2014;41(4):346–8. https://doi.org/10.1111/1346-8138.12368.
101. Rodwell GE, Berger TG. Pruritus and cutaneous inflammatory conditions in HIV disease. Clin Dermatol. 2000;18(4):479–84.
102. Bilu D, Mamelak AJ, Nguyen RH, Queiroz PC, Kowalski J, Morison WL, et al. Clinical and epidemiologic characterization of photosensitivity in HIV-positive individuals. Photodermatol Photoimmunol Photomed. 2004;20(4):175–83. https://doi.org/10.1111/j.1600-0781.2004.00101.x.
103. Furue M. Photosensitive drug eruption induced by efavirenz in a patient with HIV infection. Intern Med. 2004;43(7):533.
104. Newell A, Avila C, Rodgers ME. Photosensitivity reaction of efavirenz. Sex Transm Infect. 2000;76(3):221.
105. Treudler R, Husak R, Raisova M, Orfanos CE, Tebbe B. Efavirenz-induced photoallergic dermatitis in HIV. AIDS. 2001;15(8):1085–6.
106. Yoshimoto E, Konishi M, Takahashi K, Murakawa K, Maeda K, Mikasa K, et al. The first case of efavirenz-induced photosensitivity in a Japanese patient with HIV infection. Intern Med. 2004;43(7):630–1.
107. Bernardes Filho F, Santos MV, Carvalho FN, Castro CG, Dobao E, Lyra MR, et al. HAART: a risk factor for development of porphyria cutanea tarda? Rev Soc Bras Med Trop. 2012;45(6):764–7.
108. Verma R, Vasudevan B, Shankar S, Pragasam V, Suwal B, Venugopal R. First reported case of tenofovir-induced photoallergic reaction. Indian J Pharmacol. 2012;44(5):651–3. https://doi.org/10.4103/0253-7613.100407.

109. Diffey BL, Daymond TJ, Fairgreaves H. Phototoxic reactions to piroxicam, naproxen and tiaprofenic acid. Br J Rheumatol. 1983;22(4):239–42.
110. Stern RS, Bigby M. An expanded profile of cutaneous reactions to nonsteroidal anti-inflammatory drugs. Reports to a specialty-based system for spontaneous reporting of adverse reactions to drugs. JAMA. 1984;252(11):1433–7.
111. Figueiredo A, Ribeiro CA, Goncalo S, Caldeira MM, Poiares-Baptista A, Teixeira F. Piroxicam-induced photosensitivity. Contact Dermatitis. 1987;17(2):73–9.
112. Fjellner B. Photosensitivity induced by piroxicam. Acta Derm Venereol. 1983;63(6):557–8.
113. Al-Khenaizan S, Schechter JF, Sasseville D. Pseudoporphyria induced by propionic acid derivatives. J Cutan Med Surg. 1999;3(3):162–6. https://doi.org/10.1177/120347549900300314.
114. LaDuca JR, Bouman PH, Gaspari AA. Nonsteroidal antiinflammatory drug-induced pseudoporphyria: a case series. J Cutan Med Surg. 2002;6(4):320–6. https://doi.org/10.1177/120347540200600402.
115. Levy ML, Barron KS, Eichenfield A, Honig PJ. Naproxen-induced pseudoporphyria: a distinctive photodermatitis. J Pediatr. 1990;117(4):660–4.
116. Kaidbey KH, Mitchell FN. Photosensitizing potential of certain nonsteroidal anti-inflammatory agents. Arch Dermatol. 1989;125(6):783–6.
117. Gutierrez-Gonzalez E, Rodriguez-Pazos L, Rodriguez-Granados MT, Toribio J. Photosensitivity induced by naproxen. Photodermatol Photoimmunol Photomed. 2011;27(6):338–40. https://doi.org/10.1111/j.1600-0781.2011.00625.x.
118. Ingrish G, Rietschel RL. Oxaprozin-induced pseudoporphyria. Arch Dermatol. 1996;132(12):1519–20.
119. Cron RQ, Finkel TH. Nabumetone induced pseudoporphyria in childhood. J Rheumatol. 2000;27(7):1817–8.
120. Chishiki M, Kawada A, Fujioka A, Hiruma M, Ishibashi A, Banba H. Photosensitivity due to ampiroxicam. Dermatology. 1997;195(4):409–10. https://doi.org/10.1159/000246002.
121. Al-Kathiri L, Al-Asmaili A. Diclofenac-induced photo-onycholysis. Oman Med J. 2016;31(1):65–8. https://doi.org/10.5001/omj.2016.12.
122. Bergner T, Przybilla B. Photosensitization caused by ibuprofen. J Am Acad Dermatol. 1992;26(1):114–6.
123. Schmutz JL, Barbaud A, Trechot P. Pseudoporphyria and coxib. Ann Dermatol Venereol. 2006;133(2):213.
124. Yazici AC, Baz K, Ikizoglu G, Kokturk A, Uzumlu H, Tataroglu C. Celecoxib-induced photoallergic drug eruption. Int J Dermatol. 2004;43(6):459–61. https://doi.org/10.1111/j.1365-4632.2004.02149.x.
125. Jeter JM, Han J, Martinez ME, Alberts DS, Qureshi AA, Feskanich D. Non-steroidal anti-inflammatory drugs, acetaminophen, and risk of skin cancer in the Nurses' Health Study. Cancer Causes Control. 2012;23(9):1451–61. https://doi.org/10.1007/s10552-012-0019-6.
126. Gomez-Bernal S, Alvarez-Perez A, Rodriguez-Pazos L, Gutierrez-Gonzalez E, Rodriguez-Granados MT, Toribio J. Photosensitivity due to thiazides. Actas Dermosifiliogr. 2014;105(4):359–66. https://doi.org/10.1016/j.ad.2013.01.010.
127. Johnston GA. Thiazide-induced lichenoid photosensitivity. Clin Exp Dermatol. 2002;27(8):670–2.
128. Nakamura Y, Nemoto K, Yokoyama E, Muto M. A case of photoleukomelanoderma due to hydrochlorothiazide contained in preminent. J-Stage. 2011;73(5):482–5.
129. Robinson HN, Morison WL, Hood AF. Thiazide diuretic therapy and chronic photosensitivity. Arch Dermatol. 1985;121(4):522–4.
130. White IR. Photopatch test in a hydrochlorothiazide drug eruption. Contact Dermatitis. 1983;9(3):237.
131. Rutherford T, Sinclair R. Photo-onycholysis due to indapamide. Australas J Dermatol. 2007;48(1):35–6. https://doi.org/10.1111/j.1440-0960.2007.00324.x.
132. Burry JN, Lawrence JR. Phototoxic blisters from high frusemide dosage. Br J Dermatol. 1976;94(5):495–9.
133. Heydenreich G, Pindborg T, Schmidt H. Bullous dermatosis among patients with chronic renal failure of high dose frusemide. Acta Med Scand. 1977;202(1–2):61–4.
134. Takeichi S, Kubo Y, Arase S, Hashimoto T, Ansai S. Brunsting-Perry type localized bullous pemphigoid, possibly induced by furosemide administration and sun exposure. Eur J Dermatol. 2009;19(5):500–3. https://doi.org/10.1684/ejd.2009.0715.
135. de Fernandez Corres L, Bernaola G, Fernandez E, Leanizbarrutia I, Munoz D. Photodermatitis from triamterene. Contact Dermatitis. 1987;17(2):114–5.
136. Kanwar AJ, Dhar S, Ghosh S. Photosensitive lichenoid eruption due to enalapril. Dermatology. 1993;187(1):80. https://doi.org/10.1159/000247209.
137. Rodriguez Granados MT, Abalde T, Garcia Doval I, De la Torre C. Systemic photosensitivity to quinapril. J Eur Acad Dermatol Venereol. 2004;18(3):389–90. https://doi.org/10.1111/j.1468-3083.2004.00897.x.
138. Wagner SN, Welke F, Goos M. Occupational UVA-induced allergic photodermatitis in a welder due to hydrochlorothiazide and ramipril. Contact Dermatitis. 2000;43(4):245–6.
139. Steckelings UM, Artuc M, Wollschlager T, Wiehstutz S, Henz BM. Angiotensin-converting enzyme inhibitors as inducers of adverse cutaneous reactions. Acta Derm Venereol. 2001;81(5):321–5.
140. Frye CB, Pettigrew TJ. Angioedema and photosensitive rash induced by valsartan. Pharmacotherapy. 1998;18(4):866–8.
141. Viola E, Coggiola Pittoni A, Drahos A, Moretti U, Conforti A. Photosensitivity with angiotensin II receptor blockers: a retrospective study using data from VigiBase((R)). Drug Saf. 2015;38(10):889–94. https://doi.org/10.1007/s40264-015-0323-7.
142. Basarab T, Yu R, Jones RR. Calcium antagonist-induced photoexposed telangiectasia. Br J Dermatol. 1997;136(6):974–5.
143. Collins P, Ferguson J. Photodistributed nifedipine-induced facial telangiectasia. Br J Dermatol. 1993;129(5):630–3.
144. Grabczynska SA, Cowley N. Amlodipine induced-photosensitivity presenting as telangiectasia. Br J Dermatol. 2000;142(6):1255–6.
145. Bakkour W, Haylett AK, Gibbs NK, Chalmers RJ, Rhodes LE. Photodistributed telangiectasia induced by calcium channel blockers: case report and review of the literature. Photodermatol Photoimmunol Photomed. 2013;29(5):272–5. https://doi.org/10.1111/phpp.12054.
146. Zenarola P, Gatti S, Lomuto M. Photodermatitis due to nifedipine: report of 2 cases. Dermatologica. 1991;182(3):196–8.
147. Boyer M, Katta R, Markus R. Diltiazem-induced photodistributed hyperpigmentation. Dermatol Online J. 2003;9(5):10.
148. Scherschun L, Lee MW, Lim HW. Diltiazem-associated photodistributed hyperpigmentation: a review of 4 cases. Arch Dermatol. 2001;137(2):179–82.
149. Seggev JS, Lagstein Z. Photosensitivity skin reactions to calcium channel blockers. J Allergy Clin Immunol. 1996;97(3):852–5.
150. Miyauchi H, Horiki S, Horio T. Clinical and experimental photosensitivity reaction to tilisolol hydrochloride. Photodermatol Photoimmunol Photomed. 1994;10(6):255–8.
151. Mota AV, Vasconcelos C, Correia TM, Barros MA, Mesquita-Guimaraes J. Rilmenidine-induced photosensitivity reaction. Photodermatol Photoimmunol Photomed. 1998;14(3–4):132–3.
152. Vaillant L, Le Marchand D, Grognard C, Hocine R, Lorette G. Photosensitivity to methyldopa. Arch Dermatol. 1988;124(3):326–7.

153. Gandini S, Palli D, Spadola G, Bendinelli B, Cocorocchio E, Stanganelli I, et al. Anti-hypertensive drugs and skin cancer risk: a review of the literature and meta-analysis. Crit Rev Oncol Hematol. 2018;122:1–9. https://doi.org/10.1016/j.critrevonc.2017.12.003.
154. Chalmers RJ, Muston HL, Srinivas V, Bennett DH. High incidence of amiodarone-induced photosensitivity in North-west England. Br Med J (Clin Res Ed). 1982;285(6338):341.
155. Harris L, McKenna WJ, Rowland E, Holt DW, Storey GC, Krikler DM. Side effects of long-term amiodarone therapy. Circulation. 1983;67(1):45–51.
156. Rappersberger K, Honigsmann H, Ortel B, Tanew A, Konrad K, Wolff K. Photosensitivity and hyperpigmentation in amiodarone-treated patients: incidence, time course, and recovery. J Investig Dermatol. 1989;93(2):201–9.
157. Bongard V, Marc D, Philippe V, Jean-Louis M, Maryse LM. Incidence rate of adverse drug reactions during long-term follow-up of patients newly treated with amiodarone. Am J Ther. 2006;13(4):315–9.
158. Zachary CB, Slater DN, Holt DW, Storey GC, MacDonald DM. The pathogenesis of amiodarone-induced pigmentation and photosensitivity. Br J Dermatol. 1984;110(4):451–6.
159. Yones SS, O'Donoghue NB, Palmer RA, Menage Hdu P, Hawk JL. Persistent severe amiodarone-induced photosensitivity. Clin Exp Dermatol. 2005;30(5):500–2. https://doi.org/10.1111/j.1365-2230.2005.01820.x.
160. Trimble JW, Mendelson DS, Fetter BF, Ingram P, Gallagher JJ, Shelburne JD. Cutaneous pigmentation secondary to amiodarone therapy. Arch Dermatol. 1983;119(11):914–8.
161. Ferguson J, Addo HA, Jones S, Johnson BE, Frain-Bell W. A study of cutaneous photosensitivity induced by amiodarone. Br J Dermatol. 1985;113(5):537–49.
162. Ladizinski B, Elpern DJ. Dronaderone-induced phototoxicity. J Drugs Dermatol. 2013;12(8):946–7.
163. Armstrong RB, Leach EE, Whitman G, Harber LC, Poh-Fitzpatrick MB. Quinidine photosensitivity. Arch Dermatol. 1985;121(4):525–8.
164. Bruce S, Wolf JE Jr. Quinidine-induced photosensitive livedo reticularis-like eruption. J Am Acad Dermatol. 1985;12(2 Pt 1):332–6.
165. Wolf R, Dorfman B, Krakowski A. Quinidine-induced lichenoid and eczematous photodermatitis. Dermatologica. 1987;174(6):285–9.
166. Lang PJ. Quinidine-induced photodermatitis confirmed by photopatch testing. J Am Acad Dermatol. 1983;9(1):124–8.
167. Granados MT, de la Torre C, Cruces MJ, Pineiro G. Chronic actinic dermatitis due to simvastatin. Contact Dermatitis. 1998;38(5):294–5.
168. Holme SA, Pearse AD, Anstey AV. Chronic actinic dermatitis secondary to simvastatin. Photodermatol Photoimmunol Photomed. 2002;18(6):313–4.
169. Morimoto K, Kawada A, Hiruma M, Ishibashi A, Banba H. Photosensitivity to simvastatin with an unusual response to photopatch and photo tests. Contact Dermatitis. 1995;33(4):274.
170. Marguery MC, Chouini-Lalanne N, Drugeon C, Gadroy A, Bayle P, Journe F, et al. UV-B phototoxic effects induced by atorvastatin. Arch Dermatol. 2006;142(8):1082–4. https://doi.org/10.1001/archderm.142.8.1082.
171. Montanaro S, Lhiaubet-Vallet V, Iesce MI, Previtera L, Miranda MA. A mechanistic study on the phototoxicity of atorvastatin: singlet oxygen generation by a phenanthrene-like photoproduct. Chem Res Toxicol. 2009;22(1):173–8. https://doi.org/10.1021/tx800294z.
172. Rodriguez-Pazos L, Sanchez-Aguilar D, Rodriguez-Granados MT, Pereiro-Ferreiros MM, Toribio J. Erythema multiforme photoinduced by statins. Photodermatol Photoimmunol Photomed. 2010;26(4):216–8. https://doi.org/10.1111/j.1600-0781.2010.00519.x.
173. Gardeazabal J, Gonzalez M, Izu R, Gil N, Aguirre A, Diaz-Perez JL. Phenofibrate-induced lichenoid photodermatitis. Photodermatol Photoimmunol Photomed. 1993;9(4):156–8.
174. Leenutaphong V, Manuskiatti W. Fenofibrate-induced photosensitivity. J Am Acad Dermatol. 1996;35(5 Pt 1):775–7.
175. Machet L, Vaillant L, Jan V, Lorette G. Fenofibrate-induced photosensitivity: value of photopatch testing. J Am Acad Dermatol. 1997;37(5 Pt 1):808–9.
176. Tsai KC, Yang JH, Hung SJ. Fenofibrate-induced photosensitivity—a case series and literature review. Photodermatol Photoimmunol Photomed. 2017;33(4):213–9. https://doi.org/10.1111/phpp.12305.
177. Falkson G, Schulz EJ. Skin changes in patients treated with 5-fluorouracil. Br J Dermatol. 1962;74:229–36.
178. Horio T, Murai T, Ikai K. Photosensitivity due to a fluorouracil derivative. Arch Dermatol. 1978;114(10):1498–500.
179. Horio T, Yokoyama M. Tegaful photosensitivity–lichenoid and eczematous types. Photodermatol. 1986;3(3):192–3.
180. Usuki A, Funasaka Y, Oka M, Ichihashi M. Tegafur-induced photosensitivity–evaluation of provocation by UVB irradiation. Int J Dermatol. 1997;36(8):604–6.
181. Hague JS, Ilchyshyn A. Lichenoid photosensitive eruption due to capecitabine chemotherapy for metastatic breast cancer. Clin Exp Dermatol. 2007;32(1):102–3. https://doi.org/10.1111/j.1365-2230.2006.02245.x.
182. Shah RA, Bennett DD, Burkard ME. Photosensitive lichenoid skin reaction to capecitabine. BMC Cancer. 2017;17(1):866. https://doi.org/10.1186/s12885-017-3882-4.
183. Walker G, Lane N, Parekh P. Photosensitive lichenoid drug eruption to capecitabine. J Am Acad Dermatol. 2014;71(2):e52–3. https://doi.org/10.1016/j.jaad.2014.01.884.
184. Willey A, Glusac EJ, Bolognia JL. Photoeruption in a patient treated with capecitabine (Xeloda) for metastatic breast cancer. J Am Acad Dermatol. 2002;47(3):453.
185. Tsoussis S, Vourliotaki I, Ekonomidou F, Apostolakis S. Capecitabine as an alternative in a case of fluorouracil-induced photodermatitis. Clin Oncol (R Coll Radiol). 2006;18(2):158–9.
186. Beck TM, Hart NE, Smith CE. Photosensitivity reaction following DTIC administration: report of two cases. Cancer Treat Rep. 1980;64(4–5):725–6.
187. Buesa JM, Gracia M, Valle M, Estrada E, Hidalgo OF, Lacave AJ. Phase I trial of intermittent high-dose dacarbazine. Cancer Treat Rep. 1984;68(3):499–504.
188. Serrano G, Aliaga A, Febrer I, Pujol C, Camps C, Godes M. Dacarbazine-induced photosensitivity. Photodermatology. 1989;6(3):140–1.
189. Yung CW, Winston EM, Lorincz AL. Dacarbazine-induced photosensitivity reaction. J Am Acad Dermatol. 1981;4(5):541–3.
190. Treudler R, Georgieva J, Geilen CC, Orfanos CE. Dacarbazine but not temozolomide induces phototoxic dermatitis in patients with malignant melanoma. J Am Acad Dermatol. 2004;50(5):783–5. https://doi.org/10.1016/j.jaad.2003.12.016.
191. Cohen PR. Photodistributed erythema multiforme: paclitaxel-related, photosensitive conditions in patients with cancer. J Drugs Dermatol. 2009;8(1):61–4.
192. Hussain S, Anderson DN, Salvatti ME, Adamson B, McManus M, Braverman AS. Onycholysis as a complication of systemic chemotherapy: report of five cases associated with prolonged weekly paclitaxel therapy and review of the literature. Cancer. 2000;88(10):2367–71.
193. Beutler BD, Cohen PR. Nab-paclitaxel-associated photosensitivity: report in a woman with non-small cell lung cancer and

review of taxane-related photodermatoses. Dermatol Pract Concept. 2015;5(2):121–4. https://doi.org/10.5826/dpc.0502a24.
194. Balabanova MB. Photoprovoked erythematobullous eruption from farmorubicin. Contact Dermatitis. 1994;30(5):303–4.
195. Breza TS, Halprin KM, Taylor JR. Photosensitivity reaction to vinblastine. Arch Dermatol. 1975;111(9):1168–70.
196. Gelot P, Dutartre H, Khammari A, Boisrobert A, Schmitt C, Deybach JC, et al. Vemurafenib: an unusual UVA-induced photosensitivity. Exp Dermatol. 2013;22(4):297–8. https://doi.org/10.1111/exd.12119.
197. Goldstein J, Patel AB, Curry JL, Subbiah V, Piha-Paul S. Photoallergic reaction in a patient receiving vandetanib for metastatic follicular thyroid carcinoma: a case report. BMC Dermatol. 2015;15:2. https://doi.org/10.1186/s12895-015-0022-1.
198. Fava P, Quaglino P, Fierro MT, Novelli M, Bernengo MG. Therapeutic hotline A rare vandetanib-induced photo-allergic drug eruption. Dermatol Ther. 2010;23(5):553–5. https://doi.org/10.1111/j.1529-8019.2010.01360.x.
199. Chang CH, Chang JW, Hui CY, Yang CH. Severe photosensitivity reaction to vandetanib. J Clin Oncol. 2009;27(27):e114–5. https://doi.org/10.1200/JCO.2009.21.8479.
200. Caro-Gutierrez D, Floristan Muruzabal MU, de la Gomez Fuente E, Franco AP, Lopez Estebaranz JL. Photo-induced erythema multiforme associated with vandetanib administration. J Am Acad Dermatol. 2014;71(4):e142–4. https://doi.org/10.1016/j.jaad.2014.05.003.
201. Kong HH, Fine HA, Stern JB, Turner ML. Cutaneous pigmentation after photosensitivity induced by vandetanib therapy. Arch Dermatol. 2009;145(8):923–5. https://doi.org/10.1001/archdermatol.2009.177.
202. Fukai T, Hasegawa T, Nagata A, Matsumura M, Kudo Y, Shiraishi E, et al. Case of erlotinib-induced photosensitivity. J Dermatol. 2014;41(5):445–6. https://doi.org/10.1111/1346-8138.12476.
203. Oser MG, Janne PA. A severe photosensitivity dermatitis caused by crizotinib. J Thorac Oncol. 2014;9(7):e51–3. https://doi.org/10.1097/JTO.0000000000000163.
204. Rousselot P, Larghero J, Raffoux E, Calvo F, Tulliez M, Giraudier S, et al. Photosensitization in chronic myelogenous leukaemia patients treated with imatinib mesylate. Br J Haematol. 2003;120(6):1091–2.
205. Brazzelli V, Muzio F, Manna G, Moggio E, Vassallo C, Orlandi E, et al. Photoinduced dermatitis and oral lichenoid reaction in a chronic myeloid leukemia patient treated with imatinib mesylate. Photodermatol Photoimmunol Photomed. 2012;28(1):2–5. https://doi.org/10.1111/j.1600-0781.2011.00621.x.
206. Batrani M, Salhotra M, Kubba A, Agrawal M. Imatinib mesylate-induced pseudoporphyria in a patient with chronic myeloid leukemia. Indian J Dermatol Venereol Leprol. 2016;82(6):727–9. https://doi.org/10.4103/0378-6323.186477.
207. Yanamandra U, Sahu KK, Malhotra P, Varma S. Photodermatosis secondary to hydroxyurea. BMJ Case Rep. 2014. https://doi.org/10.1136/bcr-2014-205974.
208. Leon-Mateos A, Zulaica A, Caeiro JL, Fabeiro JM, Calvino S, Peteiro C, et al. Photo-induced granulomatous eruption by hydroxyurea. J Eur Acad Dermatol Venereol. 2007;21(10):1428–9. https://doi.org/10.1111/j.1468-3083.2007.02237.x.
209. Leroy D, Dompmartin A, Szczurko C. Flutamide photosensitivity. Photodermatol Photoimmunol Photomed. 1996;12(5):216–8.
210. Martin-Lazaro J, Bujan JG, Arrondo AP, Lozano JR, Galindo EC, Capdevila EF. Is photopatch testing useful in the investigation of photosensitivity due to flutamide? Contact Dermatitis. 2004;50(5):325–6. https://doi.org/10.1111/j.0105-1873.2004.00341m.x.
211. Yokote R, Tokura Y, Igarashi N, Ishikawa O, Miyachi Y. Photosensitive drug eruption induced by flutamide. Eur J Dermatol. 1998;8(6):427–9.
212. Lee K, Oda Y, Sakaguchi M, Yamamoto A, Nishigori C. Drug-induced photosensitivity to bicalutamide—case report and review of the literature. Photodermatol Photoimmunol Photomed. 2016;32(3):161–4. https://doi.org/10.1111/phpp.12230.
213. Sasada K, Sakabe J, Tamura A, Kasuya A, Shimauchi T, Ito T, et al. Photosensitive drug eruption induced by bicalutamide within the UVB action spectrum. Eur J Dermatol. 2012;22(3):402–3. https://doi.org/10.1684/ejd.2012.1719.
214. Llambrich A, Lecha M. Photoinduced lichenoid reaction by thioridazine. Photodermatol Photoimmunol Photomed. 2004;20(2):108–9. https://doi.org/10.1111/j.1600-0781.2004.00087.x.
215. Rohrborn W, Brauninger W. Thioridazine photoallergy. Contact Dermatitis. 1987;17(4):241.
216. Satanove A, McIntosh JS. Phototoxic reactions induced by high doses of chlorpromazine and thioridazine. JAMA. 1967;200(3):209–12.
217. Epstein JH, Brunsting LA, Petersen MC, Schwarz BE. A study of photosensitivity occurring with chlorpromazine therapy. J Investig Dermatol. 1957;28(5):329–38.
218. Matsuo I, Ozawa A, Niizuma K, Ohkido M. Lichenoid dermatitis due to chlorpromazine phototoxicity. Dermatologica. 1979;159(1):46–9.
219. Raffle EJ, MacLeod TM, Hutchinson F, Ballinger B. Letter: Chlorpromazine photosensitivity. Arch Dermatol. 1975;111(10):1364–5.
220. Bourrain JL, Paillet C, Woodward C, Beani JC, Amblard P. Diagnosis of photosensitivity to flupenthixol by photoprick testing. Photodermatol Photoimmunol Photomed. 1997;13(4):159–61.
221. Thami GP, Kaur S, Kanwar AJ. Delayed reactivation of haloperidol induced photosensitive dermatitis by methotrexate. Postgrad Med J. 2002;78(916):116–7.
222. Gregoriou S, Karagiorga T, Stratigos A, Volonakis K, Kontochristopoulos G, Rigopoulos D. Photo-onycholysis caused by olanzapine and aripiprazole. J Clin Psychopharmacol. 2008;28(2):219–20. https://doi.org/10.1097/JCP.0b013e318166c50a.
223. Al-Aojan S, Al-Khalifah A. Clozapine-induced phototoxicity: an unusual side effect of atypical antipsychotics. Case Rep Dermatol Med. 2018;2018:9242515. https://doi.org/10.1155/2018/9242515.
224. Howanitz E, Pardo M, Losonczy M. Photosensitivity to clozapine. J Clin Psychiatry. 1995;56(12):589.
225. Almond DS, Rhodes LE, Pirmohamed M. Risperidone-induced photosensitivity. Postgrad Med J. 1998;74(870):252–3.
226. Angel TA, Stalkup JR, Hsu S. Photodistributed blue-gray pigmentation of the skin associated with long-term imipramine use. Int J Dermatol. 2002;41(6):327–9.
227. Sicari MC, Lebwohl M, Baral J, Wexler P, Gordon RE, Phelps RG. Photoinduced dermal pigmentation in patients taking tricyclic antidepressants: histology, electron microscopy, and energy dispersive spectroscopy. J Am Acad Dermatol. 1999;40(2 Pt 2):290–3.
228. Walter-Ryan WG, Kern EE 3rd, Shirriff JR, Thomas JM. Persistent photoaggravated cutaneous eruption induced by imipramine. JAMA. 1985;254(3):357–8.
229. Ljunggren B, Bojs G. A case of photosensitivity and contact allergy to systemic tricyclic drugs, with unusual features. Contact Dermatitis. 1991;24(4):259–65.
230. Ram-Wolf C, Mahe E, Saiag P. Escitalopram photo-induced erythroderma. J Eur Acad Dermatol Venereol. 2008;22(8):1015–7. https://doi.org/10.1111/j.1468-3083.2007.02513.x.
231. Doffoel-Hantz V, Boulitrop-Morvan C, Sparsa A, Bonnetblanc JM, Dalac S, Bedane C. Photosensitivity associated with selective serotonin reuptake inhibitors. Clin

Exp Dermatol. 2009;34(8):e763–5. https://doi.org/10.1111/j.1365-2230.2009.03484.x.
232. Vilaplana J, Botey E, Lecha M, Herrero C, Romaguera C. Photosensitivity induced by paroxetine. Contact Dermatitis. 2002;47(2):118–9.
233. Gillet-Terver MN, Modiano P, Trechot P, Barbaud A, Schmutz JL. Fluvoxamine photosensitivity. Australas J Dermatol. 1996;37(1):62.
234. Alvarez-Perez A, Gomez-Bernal S, Gutierrez-Gonzalez E, Rodriguez-Granados MT, Toribio J. Granuloma annulare photoinduced by paroxetine. Photodermatol Photoimmunol Photomed. 2012;28(1):47–9. https://doi.org/10.1111/j.1600-0781.2011.00632.x.
235. Lin NC, Chou JY, Chen H, Chen VC. Sertraline-induced photoallergic reaction. J Clin Psychopharmacol. 2009;29(1):95–6. https://doi.org/10.1097/JCP.0b013e31819304a5.
236. Gaufberg E, Ellison JM. Photosensitivity reaction to fluoxetine. J Clin Psychiatry. 1995;56(10):486.
237. Pazzagli L, Banfi R, Borselli G, Semmola MV. Photosensitivity reaction to fluoxetine and alprazolam. Pharm World Sci. 1998;20(3):136.
238. Inaloz HS, Kirtak N, Herken H, Ozgoztasi O, Aynacioglu AS. Citalopram-induced photopigmentation. J Dermatol. 2001;28(12):742–5.
239. Vaccaro M, Borgia F, Barbuzza O, Guarneri B. Photodistributed eruptive telangiectasia: an uncommon adverse drug reaction to venlafaxine. Br J Dermatol. 2007;157(4):822–4. https://doi.org/10.1111/j.1365-2133.2007.08082.x.
240. Case JD, Yusk JW, Callen JP. Photosensitive reaction to phenelzine: a case report. Photodermatology. 1988;5(2):101–2.
241. Kanwar AJ, Gupta R, Das Mehta S, Kaur S. Photosensitivity due to alprazolam. Dermatologica. 1990;181(1):75.
242. Watanabe Y, Kawada A, Ohnishi Y, Tajima S, Ishibashi A. Photosensitivity due to alprazolam with positive oral photochallenge test after 17 days administration. J Am Acad Dermatol. 1999;40(5 Pt 2):832–3.
243. Luton EF, Finchum RN. Photosensitivity reaction to chlordiazepoxide. Arch Dermatol. 1965;91:362–3.
244. Richarz NA, Aguilera J, Castillo G, Fuente MJ, Ferrandiz C, Carrascosa JM. Phototoxic reaction to a combined oral contraceptive (levonorgestrel/ethinylestradiol). Photochem Photobiol Sci. 2017;16(9):1381–3. https://doi.org/10.1039/c7pp00160f.
245. Cooper SM, George S. Photosensitivity reaction associated with use of the combined oral contraceptive. Br J Dermatol. 2001;144(3):641–2.
246. Gomez-Bernal S, Loureiro M, Rodriguez-Granados MT, Toribio J. Systemic photosensitivity due to a contraceptive patch. Photodermatol Photoimmunol Photomed. 2010;26(4):213–5. https://doi.org/10.1111/j.1600-0781.2010.00517.x.
247. Ferguson J, Johnson BE. Photosensitivity due to retinoids: clinical and laboratory studies. Br J Dermatol. 1986;115(3):275–83.
248. Ferguson J, Johnson BE. Retinoid associated phototoxicity and photosensitivity. Pharmacol Ther. 1989;40(1):123–35.
249. Wong RC, Gilbert M, Woo TY, Kang S, Petersen C, Ellis CN. Photosensitivity and isotretinoin therapy. J Am Acad Dermatol. 1986;14(6):1095–6.
250. McDonagh AJ, Harrington CI. Pseudoporphyria complicating etretinate therapy. Clin Exp Dermatol. 1989;14(6):437–8.
251. Seishima M, Shibuya Y, Kato G, Watanabe K. Photoleukomelanoderma possibly caused by etretinate in a patient with psoriasis. Acta Derm Venereol. 2010;90(1):85–6. https://doi.org/10.2340/00015555-0746.
252. Horio T. Allergic and photoallergic dermatitis from diphenhydramine. Arch Dermatol. 1976;112(8):1124–6.
253. Schreiber MM, Naylor LZ. Antihistamine photosensitivity. Arch Dermatol. 1962;86:58–62.
254. Kim TH, Kang JS, Lee HS, Youn JI. Two cases of mequitazine-induced photosensitivity reactions. Photodermatol Photoimmunol Photomed. 1995;11(4):170–3.
255. Kurumaji Y, Shono M. Drug-induced solar urticaria due to repirinast. Dermatology. 1994;188(2):117–21. https://doi.org/10.1159/000247114.
256. Kondo S, Kagaya M, Yamada Y, Matsusaka H, Jimbow K. UVB photosensitivity due to ranitidine. Dermatology. 2000;201(1):71–3. https://doi.org/10.1159/000018437.
257. Todd P, Norris P, Hawk JL, Du Vivier AW. Ranitidine-induced photosensitivity. Clin Exp Dermatol. 1995;20(2):146–8.
258. Kastalli S, El Aidli S, Chaabane A, Amrani R, Daghfous R, Belkahia C. Photosensitivity induced by metformin: a report of 3 cases. Tunis Med. 2009;87(10):703–5.
259. Fujii S, Nakashima T, Kaneko T. Glibenclamide-induced photosensitivity in a diabetic patient with erythropoietic protoporphyria. Am J Hematol. 1995;50(3):223.
260. Sun CC. Photosensitivity due to glyburide. Photodermatology. 1988;5(1):42–5.
261. Stricklin SM, Stoecker WV, Rader RK, Hood AF, Litt JZ, Schuman TP. Persistent edematous-plaque photosensitivity observed with sitagliptin phosphate (Januvia(R)). Dermatol Online J. 2012;18(2):9.
262. Terui T, Tagami H. Eczematous drug eruption from carbamazepine: coexistence of contact and photocontact sensitivity. Contact Dermatitis. 1989;20(4):260–4.
263. Yasuda S, Mizuno N, Kawabe Y, Sakakibara S. Photosensitive lichenoid reaction accompanied by nonphotosensitive subacute prurigo caused by carbamazepine. Photodermatology. 1988;5(5):206–10.
264. Ward DJ. Carbamazepine-induced facial burns caused by a photocopier. Burns Incl Therm Inj. 1987;13(4):322–4.
265. Dogra S, Kanwar AJ. Clopidogrel bisulphate-induced photosensitive lichenoid eruption: first report. Br J Dermatol. 2003;148(3):609–10.
266. Martinez Leborans L, Cubells Sanchez L, Zaragoza Ninet V, Perez Ferriols A. Atypical photosensitivity associated with triflusal. Contact Dermatitis. 2016;75(4):245–7. https://doi.org/10.1111/cod.12609.
267. Papakonstantinou E, Prasse A, Schacht V, Kapp A, Raap U. Pirfenidone-induced severe phototoxic reaction in a patient with idiopathic lung fibrosis. J Eur Acad Dermatol Venereol. 2016;30(8):1354–6. https://doi.org/10.1111/jdv.13657.
268. Tsuruta A, Washio K, Fukunaga A, Nishigori C. Pirfenidone-induced photoleukomelanoderma in a patient with idiopathic pulmonary fibrosis. J Dermatol. 2016;43(2):207–9. https://doi.org/10.1111/1346-8138.13009.
269. Correia O, Lomba Viana H, Azevedo R, Delgado L, Polonia J. Possible phototoxicity with subsequent progression to discoid lupus following pantoprazole administration. Clin Exp Dermatol. 2001;26(5):455–6.
270. Shukla A, Mahapatra A, Gogtay N, Khopkar U. Esomeprazole-induced photoallergic dermatitis. J Postgrad Med. 2010;56(3):229–31. https://doi.org/10.4103/0022-3859.68648.
271. Balagula Y, Newman SB, Lacouture ME. Photodermatosis associated with eculizumab (Soliris): a novel monoclonal antibody directed against the complement protein C5. Am J Hematol. 2010;85(5):392–3. https://doi.org/10.1002/ajh.21672.
272. Horiuchi Y, Shimakura S. Mesalazine and photosensitivity. Am J Gastroenterol. 1999;94(11):3386–7. https://doi.org/10.1111/j.1572-0241.1999.03386.x.
273. de Rivarola Gutierrez E, Abaca H. Photodistributed lichenoid drug eruption with rhabdomyolysis occurring during leflunomide

therapy. Dermatology. 2004;208(3):232–3. https://doi.org/10.1159/000077307.
274. Lin CY, Keefe M. Mesna-induced photodistributed dermatosis. Clin Exp Dermatol. 2012;37(4):358–60. https://doi.org/10.1111/j.1365-2230.2011.04233.x.
275. Hamada K, Sawada Y, Yamaguchi T, Ohmori S, Omoto D, Haruyama S, et al. Photosensitivity due to tocilizumab presenting with erythema multiforme-like lesions. Eur J Dermatol. 2016;26(5):503–4. https://doi.org/10.1684/ejd.2016.2819.
276. Camidge DR. Methotrexate-induced radiation recall. Am J Clin Oncol. 2001;24(2):211–3.
277. Ee HL, Yosipovitch G. Photo recall phenomenon: an adverse reaction to taxanes. Dermatology. 2003;207(2):196–8. https://doi.org/10.1159/000071795.
278. Kharfan Dabaja MA, Morgensztern D, Markoe AM, Bartlett-Pandite L. Radiation recall dermatitis induced by methotrexate in a patient with Hodgkin's disease. Am J Clin Oncol. 2000;23(5):531–3.
279. Kiel PJ, Jones KL. Methotrexate-induced periorbital radiation recall. Ann Pharmacother. 2011;45(1):133. https://doi.org/10.1345/aph.1P404.
280. Korossy KS, Hood AF. Methotrexate reactivation of sunburn reaction. Arch Dermatol. 1981;117(5):310–1.
281. Stratman EJ. Chemotherapy recall reactions. J Am Acad Dermatol. 2002;46(5):797.
282. Bolognia JL, Schafferr JV, Cerroni L, editors. Dermatology. 4th ed., 2018.
283. Lowe NJ, Fakouhi TD, Stern RS, Bourget T, Roniker B, Swabb EA. Photoreactions with a fluoroquinolone antimicrobial: evening versus morning dosing. Clin Pharmacol Ther. 1994;56(5):587–91.
284. Collins P, Ferguson J. Narrow-band UVB (TL-01) phototherapy: an effective preventative treatment for the photodermatoses. Br J Dermatol. 1995;132(6):956–63.
285. Hamanaka H, Mizutani H, Shimizu M. Sparfloxacin-induced photosensitivity and the occurrence of a lichenoid tissue reaction after prolonged exposure. J Am Acad Dermatol. 1998;38(6 Pt 1):945–9.